

British physicians cool on civil defence

The British Medical Association argues that its government's recipe for defence against nuclear attack is ineffectual. But we all knew that. The question remains of what to do.

AGAINST the odds, the British Medical Association is rapidly emerging as one of the most persistent of the British Government's critics. The association has already protested at two pieces of legislation now in the parliamentary mill — the totally inadequate bill to regulate the use of data banks, which would give the authorities access to computerized personal medical records in the pursuit of crime without the consent of physicians or their patients (see *Nature* 296, 694; 1982), and the provisions of the Police and Criminal Evidence Bill that would require police physicians to carry out "body searches" (a euphemism for anal and vaginal examinations) as instructed and also empower judges to order the production of medical records in vaguely defined circumstances. Now, the association's Board of Science and Education has produced a cool report of its *Inquiry into the Effects of Nuclear War*, the effect of which will be to cast doubt on the British Government's pronouncements on civil defence. The government department principally concerned is again the Home Office, the luckless (in the sense of consistently unlucky) sponsor of all three measures.

Neither the Home Office nor the British Medical Association has picked this quarrel. The Home Office is merely following the instructions implied in the present government's legitimate decision that civil defence against nuclear attack should not indefinitely be left on one side, and has dutifully been issuing advice to individuals about the best way of securing a measure of protection against heat or fallout (blast is commonly and rightly supposed to be an unavoidable fact of nuclear war), arranging for the continuation of government by other means (devolution to regional commissioners) and giving physicians advice as to how best to prepare for serious trouble. The association, well constructed for representing to government the special interests of physicians but constitutionally the creature of its physician members, has been impelled along the road to conflict by a decision of a representative conference two years ago. The outcome of the study by a committee set up for just this purpose is all the more persuasive because it has been, as they say in trade union circles, mandated. Procedurally, the association has had the wit (and also the clout) to take formal evidence from civil servants, and to write down what its witnesses have said. Politically, it is known not to have an axe to grind, at least on this issue. Practically, the association's report is uncontentious in that it merely confirms what has been known all along — that a serious attack with nuclear weapons would be the end of the United Kingdom.

The fine print in the report is instructive and even, in its macabre way, amusing. The association's working party, in need of some estimate of how many megatons of nuclear weapons might be exploded over Britain in the case of a nuclear attack, considers that the Home Office may have underestimated in supposing a mere 200 megatons, three per cent of the warhead capacity of the Warsaw Pact, would be let off, and entertains the possibility that three times as much damage might be done. It goes on to point out the difficulties that will be faced by individuals wondering how best to protect themselves against being killed: a shelter in the middle of a house or building will be vulnerable to the destruction of the whole by blast, one near the outside will expose the occupants to more radiation from fallout radiation. There is a long catalogue of the particular medical supplies whose

general availability will be in jeopardy after a nuclear attack and a possibly constructive criticism of the Home Office's planning for a war that has not yet come in its neglect of the need for blood transfusions, if necessary by amateurs. The report notes in passing that the problem of burying the dead may not be proportionately as serious a problem as for the US Army that occupied the Philippines in 1944 because many potential corpses will have been vaporized. The load of psychiatric disorder among the survivors will nevertheless be horrendous and will go untreated. Everybody knows, of course, to whom the survivors' envy will be directed.

What, then, is to be made of the British Medical Association's report on nuclear war? One thing is clear — it has no place in that genre which seeks to frighten people into some other way of thinking or even voting. It is rather a pedestrian document, more concerned with detail than with principle. There is not even, as there might have been, a set of recommendations as to how physicians should behave in the aftermath of a nuclear attack. Should they do nothing until the intensity of ground-borne radiation has declined, hazard themselves so as to save the viable among the survivors or do the Hippocratic thing and treat the first survivor they come across? Rather by its neglect of this professional and philosophical question than by its recommendations as to how physicians should behave in an "emergency", the committee responsible declares its hand: the post-attack future cannot be foreseen by the simple extrapolation of the present.

In this poignant argument, the Home Office also has a case. Like many others, the British Government is bound to the doctrine that nuclear weapons have a part to play in military defence. To suppose from the outset that the survival of even individuals is improbable or irrelevant is to give a potential adversary a powerful advantage, the knowledge that its opponents will be fearful for their survival. That is the gap the Home Office seeks to fill. Its attempts so far to do so are the best that could have been accomplished, but are also unconvincing. It would be more beneficially persuasive of British (and other) public opinion if the present British Government were to revert to its immediate predecessor's stance and publicly acknowledge that nuclear war means death (the manner of which cannot be foretold). One consequence would be that the public interest in the progress of arms control negotiations would be enhanced. Another would be that the diversionary attention given to sober reports (like that of the British Medical Association) but also to scary documents intended to frighten would be diminished. □

The worm in the bud

Koestler, a courageous libertarian, should not have exercised his last freedom — suicide.

MR ARTHUR KOESTLER, who died last week in London in a suicide pact with his wife, was one of the small army of Central European Jews who have since the Second World War enlivened the English-speaking world and made it think. The value of his contribution to literature is beyond dispute. His novel *Darkness at Noon* (1940), born of his revulsion from the corruption of the Soviet state by Stalinism, is, however, more than merely



literature: it is an evocative indictment of governments so persuaded that they themselves can do no wrong that they disregard the liberty and even the happiness of their citizens. Like Orwell, Koestler was one whose idealism made him a republican during the Spanish Civil War and whose disillusion with what was at the same time happening in the Soviet Union led him to put humane causes such as personal freedom first. The way in which people in the West regard their governments with quizzical suspicion owes much to Koestler's powerful and beneficial influence. His personal demonstration that left-wingers can be passionately concerned with liberty has done as much to make left-wing politics respectable as a thousand more solemn social democratic tracts.

Koestler's catholic curiosity also made him a kind of polymath. *The Sleepwalkers*, his account of the long intellectual saga begun by Tycho Brahe that led to the downfall of the geocentric hypothesis, is a splendid book from which the popular hero, Galileo, emerges as one whose feet were uncomfortably made of clay. To Koestler, the quarrel between Galileo and the Church was a quarrel between a person and a powerful state about the right to believe the truth. He would have wished Galileo not to have compromised, a proper view for one in his time sentenced to death by the Spanish fascists, briefly interned by the British for the crime of being an alien in the Second World War and frequently threatened with reprisals for his influential desertion from Communism in 1938. Nevertheless, it is mystifying that, after *The Sleepwalkers* (1959), most of Koestler's brooding about scientific questions was frankly subversive. In 1966, he suggested to *Nature* a regular column, to be called "Covered Wagon", by means of which current theories would be shown to be deficient. Books such as *The Ghost in the Machine* (1967) and *The Roots of Coincidence* (1972) were respectively an antireductionist tract and an attempt to prove that the supernatural is real. It is sad that a man whose stock in trade included intelligent scepticism should have been so captivated by a little spoon-bending. It is almost as if



Koestler was looking for a cause that would allow him personally to re-enact Galileo. It was a disappointment to him that he failed.

The manner of Koestler's death is also mystifying. In the past few years, he played a prominent part in the early history of a British organization urging the social benefits of voluntary euthanasia, best known by its droll pseudo-acronym EXIT. As Parkinson's disease and leukaemia overtook him, it is natural that he should have reflected on the argument that free people should be free even to take their own lives. The trouble is that while it is possible and proper to insist that personal freedom should never be compromised by the state, the freedom to dispose of oneself cannot but be compromised by personal relationships. One consequence of Koestler's act is that his much younger wife is also dead. It will be a great surprise if the reputation of the British euthanasia society, a well-intentioned but misguided organization, is enhanced by these sad events. □

Greening of the Greens

The environmentalists have made the Bundestag. Their problems will now begin.

THERE is nothing more effective than responsibility to make people and political parties act responsibly. That is the hope prompted by the outcome of the weekend's election in West Germany, when it emerged that the new Bundestag will include 25 Greens, members of the political party that pretends to be above politics in the ordinary sense but to be concerned only with the grander issues of the environment (and the usefulness of civil nuclear power), but which is also opposed to the deployment of nuclear weapons in Western Europe (or at least in West Germany). For although incumbent Chancellor Helmut Kohl's alliance of Christian Democrats and Bavarian Christian Socialists (both of them conservative in temper) did better in the election than had been forecast, the handful of Greens in the Bundestag will probably make it necessary for his alliance to make some kind of coalition with the Free Democrats in the future government as in the last. The Greens themselves, although their faces have been set against coalitions with other parties either in the federal or the *Länder* governments, have thus killed two birds with one stone. They have become the first single-issue party to establish a major bridgehead in an elected parliament. And merely by their presence, they will force the government party to make compromises it would not have sought. Not a bad start, it will be thought. But will it make the Greens responsible?

The question is not as impertinent, or as disrespectful of the electoral process in West Germany, as it may seem. The Greens have a consistent point of view, and a legitimate one. Moreover, their influence in West Germany has been recognized to be substantial, at least since the Hamburg government voted against the development of civil nuclear power at the end of 1980, making it necessary for the regional Social Democrats unsuccessfully to seek to steal the Greens' electoral clothing in the following year. Chancellor Helmut Schmidt's government was in trouble from that point and even if the Free Democrats had not defected from his coalition, the influence of the Greens on his own party would sooner or later have put the survival of his government in doubt. So power and influence are not novelties to the Greens. Exercising them on the national stage will, however, be a novel and even dangerous experience. While the Greens may be resolved not to make political coalitions, their capacity to carry out the elements of their narrow programme will depend crucially on their willingness to trade (presumably with the Social Democrats) on specific issues.

As with other single-issue parties, the consequences may be serious, even disastrous for the Greens. The party's wish to see the pollution of West Germany abated would be laudable if it were not so extreme. The trouble with the Greens, or with some of them, is that their convictions appear to stem from a generalized conviction that the only effective way of regulating pollution of the environment is to get rid of the causes of pollution, which are for practical purposes synonymous with manufacturing industry and intensive agriculture. Much the same is true of the party's opposition to the civil use of nuclear power: this way of making electricity is absolutely an abomination, not merely an alternative source of electricity with risks and benefits that should properly be compared objectively with those of other sources. The Greens' opposition to the deployment of nuclear weapons in West Germany derives from equally over-clear principles: nuclear war in Europe would be disastrous (which is true), the risk of nuclear war is proportional to the number of nuclear weapons in Europe (which is not true) and so nuclear weapons must be got rid of wherever possible. Much of this consistent line of argument has its roots in the radical movements of the late 1960s, and is tinged with a sense of disaffection from government and from other social institutions which alone explains the ferocity with which many Greens put their view. The question they will have to decide among themselves in the next few months is whether they can moderate their position for the sake of getting something done without losing much of their support among the electorate. □

US Environmental Protection Agency

Dubious tests of loyalty for committee members

Washington

A DOCUMENT sent anonymously to Senator Gary Hart's office last week has added yet another twist to the controversy surrounding the Environmental Protection Agency (EPA). The document, a list of scientific advisers and employees of the agency with ratings of their political leanings, was said by the anonymous source to have been compiled by a member of the Reagan transition team who has since gone on to become an official of EPA.

The ratings include such comments as "at technical level rely on 120 per cent; policy level a bleeding heart liberal" (Dr Elliott Montroll, a distinguished mathematical physicist at the University of Maryland); "poison, like Sam Epstein, he is a Nader on toxics" (Dr Matthew

knowledge of the document. "I never prepared the thing or saw anything like it", he said. Cordia said that during the transition and earlier, when he was on the staff of the conservative Heritage Foundation, he did receive many suggestions from industry and conservative groups, but these were never of the negative sort that appear in the list. "Yes, some people would send in comments like 'John Doe's no good, replace him,'" but these, he said, were always unsigned notes that he immediately discarded. Cordia added that in his present position in EPA's Office of Federal Activities, he is not involved in personnel matters or in the Science Advisory Board.

Although the document contains no explicit evidence tying it to Reagan Administration officials, it was apparently common knowledge at the agency that such a list existed. Dr Roy Albert of New York University, who serves on EPA's Carcinogen Assessment Group, said, "I'd heard about this ever since the new administration came in. There were political types on the twelfth floor [the administrator's office] who had received notes from all sorts of political sources commenting on people".

Albert and one other EPA source also said they knew of a similar list, colour-coded according to political leanings, that had been drawn up about EPA senior civil service staff. "My reaction was amusement at first", Albert said, "but now outrage.

It's one of the most detestable things I've encountered."

The document also contains general comments about several of EPA's programmes:

- Radiation programme: Group is responsible for contrived public awareness for the sole purpose to scare. They should all go.

- Toxic substances programme: Get rid of them all. All known by reputation as menaces. . .

- Oceans programme: Mr Cleans committed to hard-line against ocean deposition, not there for advice, but answering the question of what can we say to shore up our position.

- Research and development programme: What have they done to earn their money? Is there a need for any? They all seem to be invidious environmental extremists.

The appearance of this list, whatever its source, will further complicate relations between Congress and EPA, inflamed in recent weeks by the suspicion that the agency in its present form is soft on pollution and by allegations that a \$1,600 million fund for cleaning up pollution has been mismanaged. One political appointee, assistant administrator Miss Rita Lavelle, has already been fired amid charges of collusion with industry polluters and perjury in her testimony before a congressional committee. The latest development is that the administrator, Mrs Anne Burford (formerly Gorsuch), who was cited in December for contempt of Congress for failing to produce subpoenaed documents relating to enforcement of hazardous waste regulations, will no longer be defended in the case by the Department of Justice. This is seen as a not so subtle hint from the White House, which is growing increasingly concerned over the political liability of keeping Burford on.

Stephen Budiansky



Meselson, a biologist at Harvard University); "clean air extremist" (Dr Edward Crandall, a pulmonary physiologist at the University of Pennsylvania); and several variations on "get him out", "a menace", "fair scientist, bad policy" and, in a reference to the endangered species that held up a major dam project, "snail-darter" type".

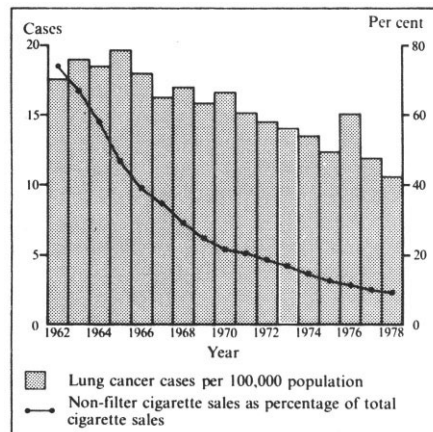
EPA officials deny that such considerations have influenced appointments to the agency's advisory committees. Dr Terry Yosie, director of EPA's Science Advisory Board, said that of those on the list who had been affiliated with the board, most still are. "I fundamentally and totally disagree with a list such as this", he said. "I think it's unethical." Yosie said he was confident that "no members currently appointed were influenced by political considerations".

The EPA official said to have drawn up the list, Louis Cordia, also disclaimed

Lung cancer incidence decreases

THE incidence of lung cancer in Britain, which accounts for 40 per cent of all male cancer deaths, is declining in men aged between 35 and 44. In 1978 there were 44 per cent fewer newly-diagnosed cases registered in males in this age group than in 1963 despite the fact that cigarette sales actually increased over this period from 109,000 million in 1963 to 125,000 million in 1978, reaching a maximum of 137,400 million in 1973. The decrease in cancer incidence is probably accounted for by the widespread changeover from non-filter to filter cigarettes, which now account for over 90 per cent of sales, and, recently, by the introduction of low-tar cigarettes. These took a major hold on the market in 1975 producing an overall reduction of 43 per cent in tar intake. According to Sir Richard Doll of the Imperial Cancer Research Fund, 91 per cent of lung cancer cases in the United Kingdom are caused by cigarette smoking and, since cancer incidence is on average 67 per cent higher in

males any reduction in the carcinogenic effects of cigarettes will bring registrations of lung cancer more in line with the downward trend seen in the incidence of all cancers. □



Source: *Cancer Statistics, Registrations 1962-1978* (HMSO £8; Imperial Cancer Research Fund; Tobacco Advisory Council).

High-energy physics

Support grows in Hamburg

IN one of the more extraordinary campaigns of the German election last Sunday, parties in Hamburg were falling over themselves to support big science — in the shape of a major new accelerator for the Deutsches Elektronen-synchrotron laboratory.

DESY (as the laboratory is called) sits smack in the middle of a Hamburg suburb, and has successfully courted the support of the Social Democrat city fathers — who pay 10 per cent of the DESY budget — for many a year. But this year, DESY benefited from the more than 1,000 jobs that its next project — a 30-GeV on 820 GeV electron-proton collider called HERA — is destined to bring Hamburg for the seven years of its construction. The Social Democrats (like everyone, no doubt, short of ideas for job creation) raised their support of HERA as a campaign issue, and the Christian Democratic Union followed suit.

In fact, the Christian Democrat science minister in Bonn, Dr Heinz Riesenhuber, went further: he made a commitment "in principle" that the HERA project will start in 1984.

The provisos are that Hamburg will pick up 15 per cent (rather than the usual 10 per cent) of the DM 300 million (£81 million) rise in the estimated price of HERA since it was mooted a few years ago (it will now cost DM 960 million, or around £260 million); and that there will be "sufficient" support from foreign countries.

Hamburg has already agreed to the 15 per cent. Sufficient foreign support has not been defined, but it could mean something of the order of a quarter the cost of HERA coming in the form of materials and equipment from countries such as France, Italy and Canada — which have been showing a strong interest in the project. Riesenhuber's firm statement will now enable supporters of HERA in these countries to take the matter further politically. DESY management is hoping that its supporters will move fast: the German budget for 1984 will be decided in June, and commitments from foreign partners will be needed by then if HERA is to start next January. Then the 6.3 km tunnel would be dug (under local houses) using conventional sewer-building technology. Seven years later HERA should give a beam, making possible a detailed survey of the structure of the proton, using the point-like electron as a precise probe rather than Rutherford used alpha particles to probe the atom.

The programme, however, depends on the successful development of superconducting bending magnets to keep the high-energy protons on course — a technology that has caused heartache and delays across the Atlantic with the ISABELLE project at Brookhaven National Laboratory, but probable success with the Tevatron at Fer-

milab. DESY has two trial designs of 6-m magnets, a prototype of one of which has just begun tests. Six experimental magnets are under construction. All are, in fact, more similar to the Fermilab magnets than to ISABELLE's. Extended involvement in superconducting techniques will interest the French and Italian governments, DESY sources believe.

Robert Walgate

● In the run-up to the election, Dr Heinz Riesenhuber also defined his position on other big projects: two, a giant spallation neutron source for low-energy materials studies and a deep crustal drilling project, have been shelved for decision "in 1985"; three, a new research reactor for the Hahn-Meitner Institut in Berlin, a new heavy ion cyclotron for Darmstadt, and a replacement for the research ship *Meteor*, will see decisions "within 12 months"; and two are already approved: an X-ray satellite ROSAT for the Max Planck Society, to start in 1987, and the large electron-positron collider LEP for CERN, Geneva, to which West Germany will contribute 25 per cent of the cost.

Landsat

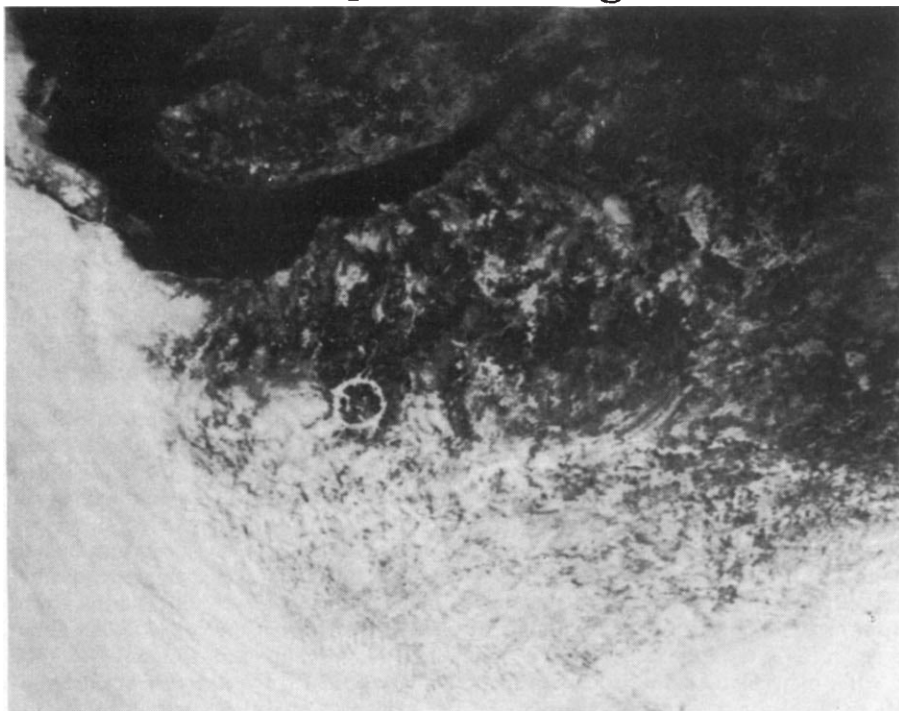
Future plans are up in the air

Washington

THE cover picture of this issue showing Washington DC was generated by a new instrument carried aboard Landsat 4, the Thematic Mapper. Flying 438 miles above the Earth's surface, this instrument can pick out features with a resolution of 30m × 30m — roughly one-quarter of an acre. Seven spectral bands, including a new middle-infrared band (1.55–1.75 μm) sensitive to variations in vegetation moisture, and significantly narrower green, red and near-infrared bands, should provide more detailed information than that available from the Multi-Spectral Scanner flown on this and earlier Landsats.

The National Aeronautics and Space Administration (NASA)'s remarkable success with this new instrument, however, comes at a time when the future of the entire Landsat programme is very much up in the air. On 31 January, NASA transferred operation of Landsat to the National Oceanic and Atmospheric Administration

Earth as seen by polar orbiting satellite



An image taken by the satellite NOAA-6, a polar orbiting imaging satellite that monitors meteorological and oceanic phenomena with a resolution of 1.1 km. Land features are also observable — in the picture can be seen the circular structure at Manicouagan, Quebec which is 65 km across, about 215 million years old, and thought by many to be an impact structure (but see also *Nature* 218, 457; 1968).

Lying within *Nature*'s London office are four large boxes of such photographs,

ready to be removed by whoever would like them. An earth scientist at the UK's Open University asked the US National Oceanic and Atmospheric Administration (NOAA-Land Sciences Branch) for a sample computer tape of such images in digital form. Rewarded for his interest by the boxes of photographs, he passed them on to us. The boxes are voluminous and heavy, and we would welcome any proposal to put them to constructive use. Those interested should write to the Editor. □

(NOAA), a part of the Department of Commerce; this is the first step toward eventual commercialization of the programme. Meanwhile, plans for future Landsats have been whittled down to a single satellite (known as Landsat D), which a back-up for Landsat 4.

The private sector's interest in taking over Landsat has been, to say the least, cool. The Reagan Administration's philosophy of getting the government out of commercial enterprises — in this case, the sale of Landsat images to geologists, agricultural researchers and anyone else who may be interested — has run into the reality of a private sector that is not keen on enterprises unlikely to make a profit. Last autumn, NOAA sought enquiries from interested buyers; it received a handful of responses (including one postcard), of which the only serious contender was Comsat Corporation.

But even Comsat is not interested in Landsat without some fringe benefits to go with it. So, to make the deal more attractive, NOAA is offering to throw in its weather satellites and a purchase guarantee of Landsat and weather data by the government. Without these bonuses, Landsat would probably seem a very poor investment. Some 50 per cent of Landsat's current users are within the federal government; and interest in Landsat data by many

users, in and out of government, is more a reflection of curiosity and subsidized prices than of a real need that could provide a market for a profit-making business.

Landsat's ability to stand on its own in the marketplace will also be encumbered by competition from the European SPOT satellite. SPOT, which is to be launched next year, will offer a finer resolution than Landsat's Thematic Mapper (10m x 10m) and will be capable of generating stereoscopic images. It will not, however, have the spectral range of Landsat.

To the further detriment of Landsat's commercial possibilities, the best data — those from the Thematic Mapper — will remain under NASA's control until 1985, reflecting the "experimental" status of this instrument (a status reinforced by the failure, NASA hopes temporary, of the mapper's transmitter last month).

On the bright side for Landsat there is a plan to have a new data relay satellite operative by the end of the summer. At present, Landsat must transmit directly to ground stations, which limits the satellite's coverage to parts of the Earth that are within range of the ground stations. Once the relay satellite is in place in geostationary orbit over the Equator, data will be relayed in real time to the White Sands, New Mexico, station for processing and distribution.

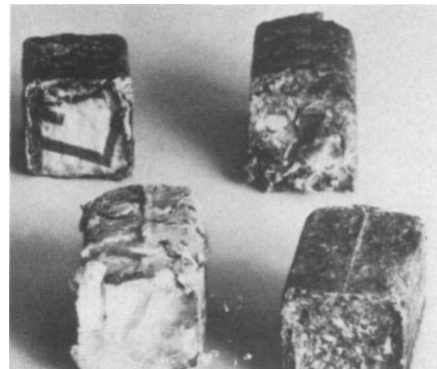
Stephen Budiansky

Artificial fuel

Waste to burn

A NEW fuel made from compressed waste is edging its way onto the British market as an alternative to solid fuels such as coal or wood. But although the fuel is ecologically sound, it seems doubtful whether it is as economical as its manufacturers claim.

From a conservationist standpoint, the fuel is ideal. It can be made from any combustible waste such as wheat straw, sewage cake or low-grade treated paper without the addition of a binding agent. Instead, the fuel cakes are produced simply by forcing pulped waste through a die, or hole, at high temperature and pressure. The resulting cubes are held together by a skin which is formed around them using a fine spray of water. This, it is claimed, means that fuel is "clean" because, unlike coal, it



Fuel from coarse mixed wastepaper (top left), fine mixed wastepaper (top right), wax paper (bottom left) and wheat straw (bottom right).

does not give rise to sulphurous gases on burning. As yet, however, the fuel is not approved for use in urban smokeless zones in Britain.

The manufacturers of the machinery that shreds and compresses the waste, Bootham North Engineering Ltd, claim that the fuel produces around 66–77 per cent of the heat of coal at about half the price and more than unseasoned wood. But this claim has not so far been borne out.

Fibrefuel, produced by Stirling Fibre Fuels from wastepaper and peat using a Bootham North system, is currently selling in Scotland and the Outer Hebrides for £65 per tonne, whereas coal sells for £90 per tonne. Allowing for the difference in heat content, the comparative price of Fibrefuel rises to £86.50 per tonne and actually becomes more expensive than coal if it has to be transported over large distances.

Despite the narrow price margin, Stirling Fibre Fuels claims that the fuel has other assets which will make it attractive to buyers. The fuel is, they say, cleaner to handle and gives a more immediate blaze than coal. Christopher Wilkin, the company's chairman, has described the first two weeks of production as "an undoubted success". However, it remains to be seen if the results achieved in a rural area which habitually uses peat-based fuels can be matched elsewhere.

Melanie Kee

Dutch science policy

Unwelcome change to come

Waalre, The Netherlands

THE administration of science policy is again a contentious issue. Until September 1981, the Netherlands boasted a Minister for Science Policy, working within the Ministry of Education and Science. Since then, the question of who should co-ordinate science policy has been the centre of a political squabble. Now the new Christian Democrat/Conservative government, in office since last November, has decided that there will be no science minister and that the Minister of Economic Affairs, Mr Gerald van Aardenne, will in future be responsible for public spending on applied research. This proposal is unpopular in parliament and elsewhere.

The proposal seems to conflict with the government's election promises that science policy would be determined not just by short-term considerations based on a calculation of industrial benefit but also in the light of long-term strategy and of social and ethical considerations. Parliamentary critics, not all of them from the largest party, the Labour Party, are complaining that the transfer of responsibility for applied research from Mr William Deetman's Ministry of Education and Science to Mr van Aardenne's economic ministry will lead to a concentration on short-term benefits at the expense of basic research.

It is not yet known what policy changes

there will be, but it has been decided that the economic ministry will follow a more market-oriented approach in micro-electronics, space research and energy research. Part of the justification for the government's organizational change is that under the previous arrangement, advisory committees would propose — and ministers would accept — research projects that were ill-founded.

Responsibility for the educational aspects of science and in particular for university research will remain with the Ministry of Education and Science. It is understood that ZWO (Nederlandse Organisatie voor Zuiver-Wetenschappelijk Onderzoek), the principal source of support for university research, will be able to back applied research projects under the terms of broader enabling legislation now being drafted.

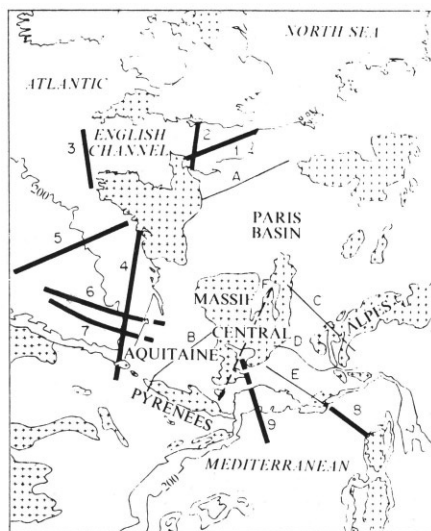
It remains to be seen whether this change will take the edge off present anxiety. With technology split from education, and with no overall coordination between ministries, the links between the universities and industry may become even more tenuous than at present. Before September 1981, the science minister was often regarded as a "snooper" meddling in their affairs. Now there may be no meddling — and no coordination.

Casper Schuurin

French geology

Seismic investigation to go ahead

FRENCH geoscientists have won approval for a large-scale seismological investigation of the geological substructure of France. The programme, to be known as ECORS (*Etude de la croûte terrestre en France par méthode sismique*), is to extend over five years. It will involve the study of five cross-



section profiles on land, each 200–300 km long and up to 40 km deep, and nine profiles at sea. A preliminary estimate puts the cost at about FF170 million (£16.5 million).

The French survey provides for symbiotic collaboration between academic and industrial geophysics. It will be administered and financed by three organizations from government and industry — the Institut Français de Pétrole (IFP), the Société Nationale Elf Aquitaine and the

Institut National d'Astronomie et de Géophysique of the Centre National de la Recherche Scientifique. The supervisory committee is under the chairmanship of C. Salle of IFP and the scientific committee under that of Claude Allègre of the Institut de Physique du Globe in Paris.

The use of seismic refraction profiling (in which explosions are used to initiate seismic wave propagation in the crust) is well established, but more sensitive and deeper crustal profiling has been made possible in recent years by seismic reflection profiling. This technique, developed principally in the prospecting industry, uses acoustic waves as in an echo-sounder. The waves initiated at the surface are reflected from regions of contrasted density (or, more precisely, acoustic impedance) and are subsequently picked up by "geophones" placed along the surface of the profile. Professor Allègre stresses that both reflection and refraction techniques can be developed further, and that a significant part of the ECORS effort will be spent on the development of theoretical techniques of inversion and seismic imaging to make the fullest use of the experimental techniques.

Work has already begun on the first profile, to be investigated this summer (profile A in the map shown). The sedimentary basin around Paris overlies geological structures dating back to the Carboniferous and Permian eras (between 225 and 345 million years ago) that preceded the opening of the Atlantic Ocean.

The subsequent profiles to be "shot" on land and sea are shown in the figure. Co-operation with neighbouring countries is to be organized.

Philip Campbell

Caspian gulf

Whose finger in the dyke?

A PLAN to stem the ecological damage caused by massive water loss from the Caspian Sea now seems to have backfired disastrously. The Kara-Bogaz dam, which separates the Kara-Bogaz-Gol gulf from the main part of the Caspian, was hailed last year as a major feat of environmental engineering. But by last autumn ecologists in the area were warning that unless steps were taken to prevent the Kara-Bogaz-Gol gulf from drying up, there would be large-scale ecological damage (*Nature* 299, 384; 1982). Now, according to the Soviet newspaper *Pravda*, the problem has been officially recognized and the State Committee for Science and Technology has agreed that drastic remedial action is necessary.

In fact, the original purpose of the dam was to let the gulf dry up. The Caspian has suffered a net annual water deficit of 15 km³, of which 5 km³ was lost by evaporation from the Kara-Bogaz-Gol, which at 160 km long and 140 km broad but only 2 to 3 m deep formed a huge natural evaporation pan.



Since the dam was completed in March 1980, the area of the gulf has shrunk from 18,000 km² to 6,000 km² and the depth is down to 50 cm. This has been disastrous for the local chemical industry, run by the Carabogazsulfat trust, which is based on sulphate-rich subterranean brines. Moreover ecologists now feel that if the gulf dries out completely, the resulting salt deposits could be blown inland, ruining fertile lands and fish farms for hundreds of kilometres.

The obvious solution would be a sluice in the dam to allow in just sufficient water to prevent contamination. Such a sluice was eliminated from the final design apparently because of disagreements over cost. Now, however, says *Pravda*, the State Committee for Science and Technology has decided that a sluice must be constructed at once.

Vera Rich

Human rights

Harassment in Estonia

AT least fifteen human rights activists in Estonia campaigning for the release of Mark Niklus, a biologist serving a 15-year sentence in a strict labour camp near Perm, were last week subjected to police search and interrogations. Several scholars were involved and one of them, the architect Lahle Parek, has since been arrested.

Mark Niklus became a keen supporter of the Helsinki Watch movement in the 1970s. He monitored and protested against breaches of human rights in the Estonian SSR, demanding in particular that the Estonian people be informed of the full text of the Moscow-Ribbentrop pact of August 1939, including the secret protocols by which the Baltic States were assigned to the Soviet Union. He was tried in 1979.

This is not Mr Niklus's first term of imprisonment — he served a 6-year sentence from 1958 to 1966, for, according to his mother, taking advantage of an interna-

tional ornithological conference in Tartu to convey to foreign colleagues snapshots "showing Soviet life as it really is". This time, however, his health has deteriorated considerably and, according to his supporters, an early release and permission to emigrate is probably the only way to save his life.

The harassment of his supporters last week suggests that the Soviet authorities will not look kindly on pleas for clemency. A few weeks ago, campaigners for Anatolii Shcharanskii were warned that reduction of sentence can be earned only by the prisoner's "repentance". And the heavy sentence imposed last week on Valerii Senderov, the Moscow activist who, among other things, monitored discrimination against Jewish applicants for university entrance — suggests that the current mood of the security authorities is one of draconian severity.

Vera Rich

US science education

Congress attempts rescue act

Washington

If you care about the trade balance, if you care about the Soviet Union getting ahead, if you care about your children, then you must do something about mathematics and science education in the United States. That was the word from the House of Representatives last week. After a seven-hour debate filled with references to Sputnik and waking up America, the House voted more than \$1,000 million for mathematics and science teaching improvements.

The overwhelming vote of 348 to 54 by the newly-elected Democrat-controlled House sent a challenge to President Reagan, who had proposed a modest \$50 million programme to recertify science teachers in his budget for next year and whose science adviser, Dr George Keyworth, has been saying for most of the past two years that the problem is a local and not a federal matter.

The President will soon be put to the test. A comparable measure is likely to pass the Senate, and although the President acknowledged that something must be done about science and mathematics education he is expected to veto the bills Congress is hatching on the grounds that they will be too costly.

The House bill (HR 1310) would give the Department of Education \$250 million next year and an unspecified sum the following year for state and local assistance for mathematics and science teaching in elementary and secondary schools. States could spend the money directly or give it to local agencies, or arrange for private industry and local universities to contribute. This provision would allow student loans for up to 15,000 undergraduate and graduate students promising to teach in elementary or secondary schools for two years for every year of scholarship received.

The bill would also give the National Science Foundation (NSF) \$100 million a year for the next five years to spend on research and grants intended to improve the quality of equipment and personnel in higher education. US universities are estimated to be short of 16,000 engineering

faculty as a consequence of competition from industry.

The bill is the product chiefly of energetic action by the powerful chairman of the Committee on Education and Labor, Carl Perkins (Democrat, Kentucky) who has pulled off a quick compromise with a rival for jurisdiction, Don Fuqua (Democrat, Florida) who wanted to give more power to NSF. Perkins is known to mistrust NSF's ability to manage large educational programmes outside its usual sphere of influence, whence the emphasis in the first part of the bill on action by the Department of Education. But Perkins has avoided the most thorny political problem: how to train more science and mathematics teachers and how to pay them enough so that they will stay.

Cause for concern

CONGRESS'S alarm about mathematics and science teaching in the United States has mounted in response to gloomy data on the problem. For example:

- In 1981, 43 states reported a shortage of mathematics teachers. A quarter of the mathematics and science teachers polled expect to leave the profession soon.

- Only a third of the nation's school districts require more than a year of mathematics or science for graduation. Seven states require none at all.

- Relatively few students entering college can major in technical fields due to poor mathematics preparation. A University of California survey of its freshmen found 92 per cent of the women and 43 per cent of the men not qualified to major in three-quarters of the university's courses.

- Student scores in mathematics and science achievement tests have dropped since 1967. Almost 60 per cent of all 17-year-olds cannot find the area of a square given the length of one side. □

Fuqua's price for the compromise with Perkins is the extra money and authority the bill would give to NSF, whose educational programmes have seesawed in the past three years. The \$20 million for teacher training proposed for next year's budget is a modest reversal of the Reagan Administration's original view that NSF should quit education. The bill's "permanent fund" of \$100 million a year is, however, intended to strengthen NSF's role in educational research and the provision of equipment in higher education.

Whatever the shortcomings of the Perkins bill, the Senate seems keen to follow suit. Congress also seems bent on testing the President's espousal of the cause last month. "We'll see if he puts his money where his mouth is", one congressional staff member said last week.

Deborah Shapley

British universities

Clean sweep at the top

THE appointment last week of Sir Peter Swinnerton-Dyer, master of St Catherine's College, Cambridge, as the new chairman of the University Grants Committee signals what is virtually a clean sweep of those responsible for administering British universities and research. Sir Peter will succeed Sir Edward Parkes, who becomes vice-chancellor of the University of Leeds on 1 July.

On the same date, Lord Flowers, rector of Imperial College London, will succeed Sir Albert Sloman as chairman of the Committee of Vice-Chancellors and Principals, while the committee's secretary general for the past five years, Mr Geoffrey Caston, will be leaving to become vice-chancellor of the University of the South Pacific in Fiji. Meanwhile, Sir David Phillips (University of Oxford) succeeds Sir Alec Merrison as chairman of the Advisory Board for the Research Councils (ABRC).

The Swinnerton-Dyer appointment is significant in many ways. First, it is a sign of open-mindedness on the part of the Secretary of State for Education and Science, Sir Keith Joseph. Sir Peter is a card-carrying member of the Social Democratic Party in whose cause he had been planning to stand for election to the House of Commons at the next election, an ambition now given up. Second, Swinnerton-Dyer has recently made an important mark on the British government's policy on universities by his advocacy (in a paper attached to last year's report from ABRC) of the urgent need to recruit young academics. This paper was the basis of the Government's decision to make up to 1,000 such posts available in the next few years.

Swinnerton-Dyer refused to be drawn last week on the policy he is likely to follow as chairman of the grants committee, promising to keep a "low profile" until July. But on past form, he is likely to be even more dedicated than his predecessors to the pursuit of excellence in teaching and research, more willing than they have been to encourage flexibility within British higher education as a whole, likely to fight more fiercely for the autonomy of the grants committee and its dependent universities and more likely to say in public things his predecessors have said in private.

In an address on his retirement as vice-chancellor of the University of Cambridge in 1981, Swinnerton-Dyer argued that the British Government had rightly sensed that change was needed within the British university system without knowing what reforms were needed, and that the apprehension of academics, while natural, should not impede reform. "For all we know, the caterpillar may view with equal apprehension his inescapable transformation into a butterfly." □

International comparisons of engineering baccalaureate degrees

Country	Engineering degrees, % of all degrees	Total engineering degrees
United States	6	59,200
West Germany	6	5,000
United Kingdom	12	10,900
Japan	19	73,500
Soviet Union	39	319,000

Source: National Science Board Commission on Precollege Education in Mathematics, Science and Technology.

Plant biotechnology

British venture plans mature

THE British Technology Group (BTG) is likely to announce "shortly" plans for a new agricultural genetics company. The company, which has not yet been named, will have first refusal options on ideas originating from some of the research funded by the Agricultural Research Council (ARC). It will thus play a similar role to that of Celltech with the Medical Research Council.

Financial backing for the new company is expected from Ultramar, the British-based international oil company, and Advent Capital Ltd. ARC has approved the idea in principle and an announcement is expected as soon as details of the research areas to be offered to the new company have been settled.

The new company was first mooted some 18 months ago, but a variety of financial and personnel problems hindered early development of the idea. Government aid which had been sought was apparently not forthcoming, and the private sponsors were originally looking for proposals which could be brought to profitability within five years. However, the scientists who were approached apparently felt this to be an unrealistic aim. It was thought that more basic research in plant genetics would be needed before this goal could be contemplated, and the "five years to profitability" requirement was dropped. Dr Richard Flavell, of ARC's Plant Breeding Research Institute at Cambridge, is now thought to have agreed to act as the new company's chief executive subject to details being finalized with ARC. An administrative director has also been found.

Mr Roger Hay and Dr Roger Cox of BTG last year set up a small holding company, New Plant Products Ltd, to carry out pilot studies for the proposed company. New Plant Products Ltd will be incorporated within the new company when this is formed. One research area currently

being investigated is the development of rape seed/jojoba hybrids produced from fused cells which have superior oil properties. Other ARC work which may form the basis of the new company's first products

International biotechnology

UN centre to be based in India?

INDIA is emerging as the most likely host for the international centre for genetic engineering and biotechnology, proposed last year by the United Nations Industrial Development Organization (UNIDO). Canada and Sweden, both at one time strong contenders, have withdrawn from the running.

The UNIDO proposal was discussed by representatives of thirty-five interested countries in Belgrade last December. (The United Kingdom sent only an observer, the United States not even that.) The centre is planned to have at least 50 scientists, 26 postdoctoral fellows, 100 visiting trainees and an annual budget of \$8.6 million.

Governments interested in accommodating the centre have been asked to submit a proposal to a UNIDO committee due to meet on 14 March to consider the proposals. After visits to the countries concerned, the committee will make a recommendation to a ministerial meeting this summer that should settle the future of the centre. Unless there are any last-minute applications, the list of contenders will be Belgium, Cuba, Italy, India, Pakistan and Thailand. The most likely outcome, at least according to some Swedish scientists involved with the project, is that the centre will end up in India, supported by Swedish foreign aid money and with a small affiliated centre in Uppsala.

Before the meeting in Belgrade, it was hoped in Sweden that the centre would be in Uppsala, where both the Biomedical Centre and the Wallenberg Laboratories are deeply involved in biotechnology. These hopes were based on the belief that it would be recognized that the centre needs to be located where top-class scientists are prepared to live — and that Sweden was one of the most acceptable of developed countries.

Faced, however, with proposals from India and other developing countries, Swedish politicians, led by the Prime Minister Olof Palme, have decided that Sweden should not compete. At least two problems are thereby avoided: that Swedish aid organizations would not support the centre in a developed country and that the high tax-free salaries of the centre would have been an attraction, an irritation or both to Swedish biotechnologists.

If Sweden is prepared to provide financial support for the centre in India, the package is likely to be the best on offer this

concerns the genetic engineering of *Rhizobium* and mycorrhizal inoculants for white clover, used to help add nitrogen to soil in upland reclamation schemes. New Plant Products Ltd is already manufacturing conventional *Rhizobium* inoculants at ARC's Rothamsted Field Station. Mr Hay is confident that the new company will generate significant revenues "within the next five years".

Tim Beardsley

summer. As proposed, the host country will have to provide the building for the centre but funds will depend on what UNIDO can arrange. Even if the location and financing can be settled in the summer, UNIDO may be faced with serious problems of staffing and policy making.

Peter Newmark

Bio-Japan in Bethesda?

Washington

OTSUKA Pharmaceutical Co. Ltd plans to become the first Japanese drug company to establish a research facility in the United States. Otsuka, which together with a sister company ranks second in drug sales in Japan, hopes to begin construction of the 30,000 square foot facility at a site in Maryland by late summer. Research would focus on genetic engineering.

The company's representative, William McHale, says that Otsuka is setting up in the United States to "take advantage of the personalities who are very active in this field" and because genetic engineering research had been "held back by political and legal impediments" in Japan.

Although the exact site has not been settled, the Montgomery County, Maryland, economic development office confirms that Otsuka has been negotiating a lease for a site at the county's Shady Grove Life Sciences Center, a biomedical industrial park in Gaithersburg, Maryland. McHale says Maryland was chosen among several other possible locations in the United States for its "scientific climate". "The large scientific community which is here because of the National Institute of Health (NIH) makes this area attractive", he said.

Rumours about Otsuka's plans have been circulating at NIH in recent weeks, leading to some speculation that the company was planning to poach on NIH's expertise through what will be largely an information-gathering office. The Gaithersburg site is about 10 miles from NIH. But McHale says the facility will be primarily a research centre, not directly involved in either information gathering or manufacture of products.

Otsuka has not yet chosen a director for the new laboratory.

Stephen Budiansky

Clouded future

It now seems to be understood that the British Technology Group will lose the right of first refusal on patentable inventions made with public funds when the results of the government's review are published some weeks from now. The intention seems instead to be that universities and other publicly supported institutions should be free either to exploit inventions on their own account or to offer them to the group.

The extent to which the organization will continue to function as a publicly-financed source of venture capital is, however, yet to be decided. The possibility, however remote, that it may cease to exist has nevertheless cast a cloud over negotiations such as those with ARC. □

Biotechnology

Silver cloud with a leaden lining

Washington

THE market for biotechnology stocks has been strong in recent months, as recent *Nature* stock indexes have shown (this month's is shown below). But this silver cloud may have a dark lining for the fledgling industry: showers of cash from eager investors may not help the companies adjust to the realities of the business world.

An estimated 200 companies have been founded in recent years in the belief that recombinant DNA technology will revolutionize everything from cancer diagnosis to the extraction of metals. But since there are virtually no recombinant DNA engineered products yet on the market, there is no objective measure of the companies' worth.

When things have been good — as when, in October 1980, Genentech of South San Francisco offered its stock for public sale at \$39 per share and saw it rise to \$80 in a few hours — they have been very good. But when things have been bad, as in early 1982, the companies have just limped along.

Soon, Biogen NV, one of the first and most prominent biotechnology companies, plans to offer its stock for public sale. The offering of 2.5 million shares, with a hoped-for price of between \$22 and \$26 a share, will thus be a test of how the market feels about biotechnology. The offering could bring in more than \$55 million in a single day and could be a heady prize for its founders, including former Harvard professor Walter Gilbert, who bought into the company in 1978 for \$4,750 and began consulting at a rate of \$500 per day. That was before Gilbert won the Nobel prize in 1980, before the biotechnology boom started and before Harvard made Gilbert choose between his Harvard post and Biogen. He chose Biogen.

Biogen's prospectus indicates that in 1982 Gilbert, who is chairman of the board of supervisory directors, the scientific board and the board of directors of the company, received \$274,000 in remuneration. If stock prices hold at \$22 when the company goes public, his 600,000 shares will be worth an estimated \$13.2 million. At present, the largest shareholder is the International Nickel Corporation (Inco), which has 20 per cent of the stock. Monsanto and Schering Corporation have 12.5 per cent each.

Biogen may become the first company to have its recombinant DNA engineered interferon on the US market. Schering is currently running clinical trials of leukocyte interferon made with Biogen's methods and says it is pleased enough with the way the clinical trials are going to plan a major production facility; the interferon could be marketed as soon as 1984.

Biogen is competing with Genentech on immune interferon and the production of human insulin. Biogen has an agreement with Novo Industri, the Danish producer

of animal-based insulin, for the production and testing of its insulin. Gilbert's company is also working on several proteins, including factor VIII for treating haemophilia, human serum albumin for transfusions and tissue plasminogen activator to dissolve blood clots. Through an agreement with Inco, it is working on organisms to extract non-ferrous metals from low-grade ores.

But some observers of biotechnology are concerned that companies like Biogen which plan their own production of recombinant DNA products will face huge demands for cash. Moreover, the need to impress potential investors is driving many into high-glamour, big-market areas such as cancer diagnosis or herpes treatment when they might do better to develop less ambitious products for the sake of a positive cash flow.

Biogen (registered in the Netherlands Antilles but with offices in Geneva, Zurich, Brussels and Cambridge, Massachusetts) has had net losses each year since 1978: the loss in 1982 was \$4.5 million.

The boom market is enabling many companies to make public offerings, covering chronically negative cash flows. Says one analyst at Arthur D. Little: "One of the disturbing things is that all the money is coming in to fund anticipated products. A lot of these products are going to end up not being successful."

Indeed, there has been a rash of stock offerings by companies with negative cash flows. And many companies are making deals with much larger companies, either to acquire venture capital or to buy produc-

tion and marketing expertise.

For example, the Martin Marietta Corporation has just bought a 20 per cent interest in Molecular Genetics, a Minnesota company specializing in animal health care and agricultural applications. Molecular Genetics reported second-half losses in both 1981 and 1982, and is now hoping to raise \$18 million through a stock offering.

Hybritech, a company that reported net losses of \$7 million in 1982, made a stock offering late last year to raise cash (see *Nature*, 13 January, p.105). The company makes medical diagnostics kits and carries out research. However, some companies, like Bio-Response, manage to conduct their research and development without running in the red.

Some analysts believe that at \$22 per share, Biogen may be slightly overvalued. Likewise Genentech is selling at \$64 per share although big profits will depend on Food and Drug Administration approval of its products, which could take years.

Some say that the Genex Corporation, of Rockville, Maryland, is a good buy and living within its means. It has approximately 11 million shares outstanding and trades at around \$17 per share. On the other hand, Genex is planning to produce its own products and "will need \$30 to \$40 million in the next few years to build construction facilities", one analyst said. Like so many other companies, Genex is signing up big company users: one recent deal for industrial enzymes was with Bendix Corporation.

The strong market is a boon to the companies, providing the cash they sometimes need badly. But, even with fresh cash, the companies face many adjustments to come to terms with investors' expectations.

Deborah Shapley

Nature index of biotechnology stocks

12-Month high	12-Month low	Company	Close previous month	Close 25 Feb.	Change
57*	16 1/8	A.B. Fortia (Sweden)	49	52	+3
8	2	Bio-Logicals (Canada)	3 3/4	3 1/4	-1/2
13*	3 3/8	Bio-Response (USA)	10 3/4	11 1/8	+ 3/8
16 1/8 *	7 3/4	Cetus (USA)	14 3/8	14 1/4	- 1/8
14 1/2	6 1/8	Collaborative Research (USA)	12 3/8	14 1/2	+ 1 1/8
23 1/8 *	5 3/4	Damon (USA)	19 3/4	23 1/8	+ 3 5/8
31*	8 1/4	Enzo-Biochem (USA)	28	30 1/4	+ 2 1/4
28	6 1/8	Flow General (USA)	14 3/4	17 1/4	+ 2 1/2
69 3/4 *	26	Genentech (USA)	53 3/4	64 1/2	+ 10 3/4
12 1/2 *	2 1/4	Genetic Systems (USA)	11	10 7/8	- 1/8
17 7/8 *	7	Genex (USA)	16 3/4	17 3/8	+ 7/8
27 3/4	9 5/8	Hybritech (USA)	26 1/4	27	+ 3/4
18 1/2	5	Molecular Genetics (USA)	14	18 1/2	+ 4 1/2
52 1/4 *	34 7/8	Novo Industri A/S (Den)	49 3/4	51 5/8	+ 7/8
27	8	Monoclonal Antibodies (USA)	19 1/2	21 1/2	+ 2

The *Nature* Biotechnology Stock Index for February 1983 stands at 195.1 compared with 181.7 last month. Base is 100 as of 25 June 1982. The previous index appeared in *Nature* 10 February, p.459. Close of month prices are the closing prices on the last Friday of each month. Where stocks are traded over the counter, the price quoted is the bid price. Where stocks are traded on the American and New York Stock Exchanges, the price quoted is the transaction price. Data from E.F. Hutton Inc.

*New high or low for this calendar year.

Physics research

SIR — "Basic physics in doldrums" (*Nature* 300, 571; 1982) summarized the findings of a study, "Trends in Research Output and Funding" (*Physics Today*, p.9 November 1982) which I conducted in collaboration with Harold Weinstock, Francis Narin and Samuel R. Reisher. While the *Nature* article provides excellent coverage of a number of the salient findings of our study, the opening sentence attributes to us a judgement which we were careful not to make, that "Basic physics research in the United States is declining in quality compared with Europe . . ." In point of fact we applied no quality measures in our study. Rather, we compiled data on (1) the numbers (quantities) of papers published in *Physical Review Letters* and in *Applied Physics Letters* by various performing sectors and (2) the numbers (quantities) of papers attributed to various funding sources. The findings led us to comment that "We view these trends with concern and believe they correspond to a reduction — in real terms — of US activity in basic physics since the late 1960s". The emphasis here is on the reduction in the quantity (not quality) of activity.

The *Nature* article also asserts that "The ONR study speculates that this dramatic shift in foreign contributions might be caused by editorial policy". In actuality, referring to *Physical Review Letters*, we commented only that "The total number of papers published per year by all sources rises until 1968 and thereafter remains relatively constant at approximately 1,000 papers per year, presumably a consequence of editorial policy". Although the presumption in the last phrase proved to be incorrect, our statement contains no speculation that editorial policy might have caused a shift in foreign contributions.

It is recognized that varying interpretations of our data are possible. For readers who might wish to draw their own conclusions from the original data I shall be pleased to provide, on request, copies of a more comprehensive version of the report than that which appeared in *Physics Today*.

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Xenology disputed

SIR — In proposing the word xenology to collectively describe extraterrestrial studies, R.A. Freitas Jr (*Nature* 13 January, p.106) notes that Reynolds¹ used this word to describe the study of xenon isotopes, but claims that this use of the word xenology "has negligible currency in the literature". We disagree.

Reynolds¹ defines xenology as "the detailed study of the abundance of Xe isotopes evolved from meteorites . . ." The word now is used also for all terrestrial and extraterrestrial (including the Moon

and Mars) studies of xenon isotopes²⁻⁵. The element xenon has nine stable isotopes that can have a variety of origins. As noted by Pepin²: "The cornerstone of xenology is the experimental observation that Xe isotopic ratios differ in significant and complex ways among naturally occurring samples". There are more than 20 research groups in at least eight countries that measure and use xenon isotopic abundances in studies of terrestrial and extraterrestrial samples. Many of the scientists in these groups frequently use the word xenology. The word *Xenologie* is in the title of a German article³; the English abstract uses xenology. A recent paper⁴ is entitled "Terrestrial xenology". A subchapter of a new book⁵ is "Unsolved problems in xenology".

The failure of Mr Freitas to find xenology as a subject category is not surprising, as many words formed by adding -ology to a noun are filed under the category of the noun itself. Thus works on xenology are found under xenon. Having clearly refuted Mr Freitas' claim that xenology has "negligible currency", and shown that it is well established in referring to studies of xenon isotopes, we urge that xenology not be used for any other field.

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1. Reynolds, J.H. *J. geophys. Res.* 68, 2939-2956 (1963).
2. Pepin, R.O. & Phinney, D. *Moon and Planets* (submitted).
3. Hintenberger, H. *Naturwissenschaften* 59, 285-291 (1972).
4. Staudacher, T. & Allègre, C.J. *Earth planet. Sci. Lett.* 60, 389-406 (1982).
5. Kuroda, P.K. *The Origin of the Chemical Elements* (Springer, Berlin, 1982).

SIR — Robert A. Freitas Jr's letter (*Nature* 13 January, p.106) is an eloquent plea for a name we do not need. While a universally accepted collective term could be useful for studies on extraterrestrial life, given their largely common factual and theoretical bases, attempts to bring some or all of non-solar planetary physics, pre-biotic geology and other disciplines into this category is merely verbal colonialism, and does not reflect the organization of knowledge or research effort. The term "xenology" is unwanted and misleading, implying a grand unification absent in fact.

It also fails to suggest "extraterrestrial studies", rather meaning "studies of the unexplained/unusual/strange" through common technical usage of the "xen" root. "Xenology" could thus be replaced by "science" in most contexts.

WILLIAM BAINS

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Down to Earth

SIR — May I as organizer of the Royal Society discussion meeting on the Earth's core, protest mildly at your comment

(*Nature* 23 December 1982, p.681) on the proceedings¹. You say "Shockingly it makes no mention of Ramsey's theory . . ." that the core is not iron or iron alloy but a metallic phase of the silicates of the Earth's mantle induced by the high pressure. You are less than fair to the distinguished geophysicists who contributed to this part who may well have taken to heart Professor Lyttleton's recent admonition to geophysicists (in a review² on comets . . .) to adhere to Occam's razor which, as he so clearly expounds, "enjoins our scientists to include no hypotheses not absolutely required . . .".

Neither experimental nor theoretical work at high pressure gives any evidence that such a phase change would occur at the pressure in the Earth's core, or that the density jump would be as large as is observed, or that the phase change pressure will change in the way Professor Lyttleton requires in his Earth contraction model. Nor is an Earth contraction hypothesis relevant to explaining tectonics on the Earth as we now know it looks as a result of palaeomagnetic, geological and geophysical studies over the last quarter of a century.

Nor is there any reason now from work on the Sun and carbonaceous chondritic materials to doubt (as there once was) that the cosmic abundance of iron is such that an iron core is reasonable. Had you read the Royal Society publication, instead of being shocked by it, you would have noticed that a correlation between the irregular fluctuations in the length of the day and the relative rotation of the core and mantle, as measured by the geomagnetic westward drift, means that interchange of angular momentum between core and mantle is occurring on the time scale of decades (by electromagnetic coupling) and may very well do so on much longer time scales. I explain that there is some archaeomagnetic evidence for this and that it would explain the acceleration over the past 2,500 years, as inferred from the ancient eclipse data, recently put on a satisfactory basis by F.R. Stephenson.

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ONLY Lyttleton carries a torch for the Earth-contraction hypothesis, while the simplest version of Ramsey's theory (silicate to silicate phase transition) is, as Professor Runcorn says, ruled out by observation. But in his introduction to the Royal Society meeting, Dr J.A. Jacobs said " . . . we know more about the interior of Jupiter than we do about that of the Earth. I should like to see more experimental work at high pressures and temperatures simultaneously . . . particular attention should be paid to phase transitions in mantle materials and to the nature of the core-mantle boundary . . ." I agree, and would not be surprised if the result were the discovery that the mantle-core boundary is less a manifestation of chemical differentiation than is now assumed. — Editor, *Nature*

Planetologists of the Solar System, unite

European planetary scientists are up in arms for lack of spacecraft and their US colleagues are no better off. They should get together and decide what they want to do.

THAT turbulent body of men and women consisting of Europe's planetary scientists is once more up in arms, its anger on this occasion directed against the European Space Agency. The issue is at once complicated and simple. The agency, being by constitution a consortium of mutually-jealous governments, conducts its affairs by means of a complicated interlocking hierarchy of advisory committees. The committees necessarily advise the council, whose decision is constitutionally final, and whose awareness of what the agency has to spend is necessarily more acute than that of its advisers. At the council's next meeting, two weeks from now, the space agency will be advised to put its next pot of money into infrared astronomy and to neglect the Kepler mission, a scheme for sending an orbiting satellite to Mars (see *Nature* 24 February, p.647). Most probably, it will follow the advice proffered. There will be two consequences — European infrared astronomy (something of a corner in a large market) will prosper and the geophysicists of the Solar System (which is a contradiction in terms) will be even more offended.

The simple explanation of this state of affairs, where European planetary scientists are concerned, is too simple. There are too few launches of European satellites and other rocket-borne devices in prospect to satisfy legitimate claimants. As things are, the European Space Agency is able to plan for one exploit of a scientific character every eighteen months or so. Chauvinistically but also to save costs, it is biased towards the use of the Ariane rocket as a launching vehicle, but can from time to time be bullied into paying for an American Thor-Delta instead, as now arranged for this summer's launch of the European X-ray satellite called Exosat (see *Nature* 3 March, p.4). Planetologists complain that they are short-changed by the committees, but even solar physicists and astrophysicists argue that they could be more productive if there were more opportunities for extraterrestrial observations.

The more complicated answer is almost impossibly so. The most tangible part of it is the cost of planetary missions. The standard cost of a typical instrumental expedition such as Kepler is \$500 million or thereabouts, comparable with the cost of many sizeable particle accelerators or the annual operating budgets of even quite large universities. Astrophysically-directed Earth satellites, on the other hand, may

often be an order of magnitude cheaper; much depends on whether the launcher and some of the instrumentation can be bought off the shelf. Although the harvest of understanding won by the latest Voyager spacecraft to Jupiter, Saturn and more distant points is still being brought in (*Nature*, *passim*) even the fondest Congress will not send them up as if they were fireworks on 4 July. President Reagan's budget for the coming financial year includes \$300 million for an instrument to map the surface of Venus by means of radar, the only substantial investment in planetary science now made public. The explanation of these high costs is not far to seek: the greater the distance, the greater the need for both broadcasting power (and thus of launching weight) and for pre-tested reliability. Planetary scientists could do themselves a service by worrying about costs.

The less defensible part of the planetologists' case, but also the more interesting, is that implied by the question "What is it for?". There are three kinds of responses, of which the grandest is the simple statement that planetary science is meant to explain how the Solar System came into being. Planetologists should therefore note what outsiders sense to be the case — that since measurements of planets beyond the Moon began to accumulate more quickly than their data could be assimilated, more than a decade ago, theorizing about the origin of the Solar System has tailed off. The people concerned are either too busy telling what the data are in all those reels of tape, or are in awe of them. Planetology is also defensible on the grounds that phenomena elsewhere may illuminate some occurring closer at hand, as an understanding of the Red Spot of Jupiter may yet help to explain the "blocking" of anticyclones in temperate terrestrial latitudes, and because there are probably many undiscovered phenomena yet to surprise us.

How, in these circumstances, should planetary scientists conduct themselves? Complaining at the committee procedures of the European Space Agency is the most obvious but the most negative course to follow. So long as the cost of planetary scientists' ambitions when added up outstrip the present cost of supporting the remainder of academic science, there is very little chance that they will be satisfied. A better tack would be to demonstrate to the rest of the scientific community (but also to legal entities such as the US Con-

gress and the European Space Agency) that the data gathered in previous planetary missions are being used to the fullest. In the United States, unfortunately, this goal is compromised by the circumstance that the cost of launching something, almost *anything*, is more visible than the cost of analysing whatever data may be gathered. The American Astronomical Society has complained of next year's US budget, the Venus Radar Mapper notwithstanding, that an extra \$11 million is needed for the expeditious analysis of data already piled up by earlier projects. In Europe the same complaint is nevertheless valid.

So why should not the United States and Europe pool their resources on the analysis of past data about the Solar System, and on the planning of future projects? There is nothing but ephemeral chauvinism to deny that question. What planetary science most urgently needs is an international institute of planetary science, a free-living centre of research with access to data from everywhere. The National Aeronautics and Space Administration in the United States is in a mood for a deal along these lines, but would probably take offence if the centre were not alongside the Jet Propulsion Laboratory in California. The European Space Agency is in the same case but would prefer a site in the Low Countries. Planetary scientists, who are temporarily a thorn in the flesh of such agencies, should work out among themselves how the enterprise should be organized.

Planetary scientists must also work out among themselves some means of regulating their internal business in a seemly way. As things are, people complain that they are shy of putting forward imaginative proposals to the advisory committees for fear that their ideas will be stolen, if not by a fellow-national then by somebody else. The consequence of such theft is not merely injured pride but a potential loss of business for a home laboratory. This, too, is a problem that could be made to go away if there were a sufficiently independent international centre for planetary science, one sufficiently well-endowed with people to draw up a systematic and persuasive programme for the exploration of the Solar System by means of spacecraft carrying instruments. As things are, both in Europe and the United States, the prizes (if any) go to the clever instruments. Understanding where the Solar System came from is a secondary consideration. □

Interplanetary travel

A puff of wind for the solar sail?

from L.D. Friedman

ALTHOUGH out of favour with the space agencies, the idea of solar sailers coursing through the Solar System is being kept alive by enthusiasts on both sides of the Atlantic Ocean. The World Space Foundation, a non-profit public subscription space group in the US, is building a prototype sailing vehicle in preparation for a Space Shuttle or Ariane test, tentatively scheduled for 1986. A 260 m² sail has been successfully fabricated, packaged and deployed in a ground test.

In France a similar group of space enthusiasts has challenged the World to a solar sailing race to the Moon. The engineers at Union Pour la Promotion de la Propulsion Photonique (UPPP) have designed and built a scale model of a solar sail for their entry in the proposed race. They hope to obtain a ride on Ariane. Like the members of World Space Foundation, many of the volunteers working with UPPP are professional engineers and scientists with industry and space agencies. The president of World Space Foundation, Robert Staehle, is an engineer at NASA's Jet Propulsion Laboratory. Anne Marie Mainguy, new president of UPPP, is with ONERA.

At last October's meeting of the International Astronautical Federation, a third group from Prague also put forward plans. They are doing theoretical studies and building model sails to study dynamics of the vehicle.

Interest in the solar sail has remained extraordinary ever since NASA rejected as too risky the idea of using a sailing vehicle to rendezvous with Comet Halley (current planned missions to the Comet by Europe, Japan and the USSR will all fly-by at speeds of approximately 70 km s⁻¹ instead of being able to rendezvous, that is, match speed and position). The Jet Propulsion Laboratory studied two sail designs: the Heliogyro, a spinning vehicle which derived its structural rigidity and control from helicopter-like blades; and a square sail rigged like the sails of an ocean ship with spars, stays, winches and vanes for control and structure. The Heliogyro design was the finalist in that study although it defied intuition at the time. The present groups, working their smaller plans, now are using square sail designs.

Although the JPL study concluded that sailing was feasible, and perhaps advantageous for operations in the inner Solar System, the research work never found a home in NASA and was dropped. Study of the basic technology of thin films, materials, control of large vehicles and

structural dynamics has continued, however. The sail was a victim in part of bureaucratic scepticism and inertia, but more so of the decline in planetary exploration. Not only it, but also the electrical propulsion schemes of ion drive and nuclear drive were dropped from NASA plans. With the pace of exploration of the Solar System cut from one dozen missions per decade to one or two, there is simply no near-term need for low thrust propulsion — at least not until basic reconnaissance and exploration of the Solar System objects are complete.

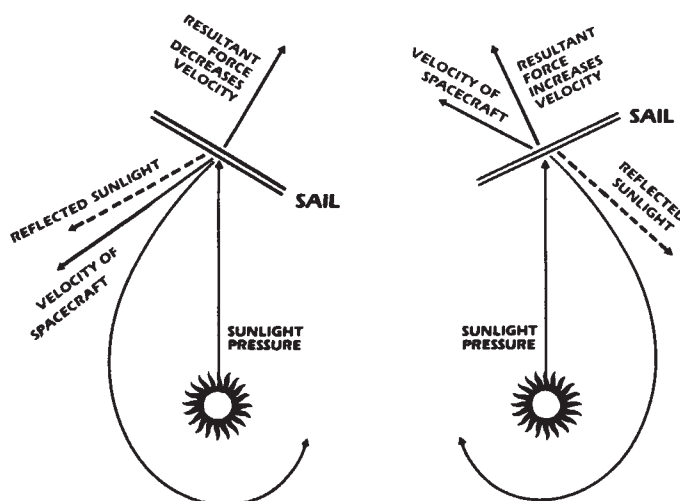
But ideas such as a race to the Moon, and volunteers joining to build a Shuttle test vehicle and then finding financing to go to an asteroid, and students in a non-space-faring nation building and researching a new vehicle design, keep the idea of the sail alive. Operation in near-Earth orbit, as would be required in a Moon race, is not the best way of using the sail. It must be continually manoeuvred as it goes around the Earth in a lazy spiral to face (approximately) the Sun. Most sail enthusiasts look to the applications of the vehicle as an interplanetary shuttle. In this capacity it offers re-usability, no fuel consumption, efficiency and large mass cargo capability.

The sail is a low-thrust vehicle generating only about 10⁻⁴g acceleration (10⁻³ m s⁻²). That's why a slow spiral is necessary in

Earth orbit unless there's a large chemical rocket push. On interplanetary trajectories the small acceleration gradually builds up a high velocity. Sunlight pressure is the basic force, applying about 9 Nt km⁻² at the Earth's distance. Thus, a large (say 0.25 km²) reflective sail can have an acceleration of about 9 mm s⁻² divided by the mass per unit area of the sail ('load'). The JPL-designed sail vehicle had a total load of 5 g m⁻² (with the sail itself being 1.2 g m⁻²). Future designs, such as those developed by Eric Drexler at Massachusetts Institute of Technology, involve manufacturing the sail in orbit. This might reduce the load by a factor of three to five.

Whereas an ocean sailer operates at the interface of the wind and water, a space sailer derives its steerability by operating at the 'interface' of sunlight and orbital velocity. As the accompanying diagram shows, the sail can be made to spiral inwards or outwards in the Solar System by either adding or subtracting orbital velocity.

Managers in the space community are still sceptical about the sail's future. Both the World Space Foundation and UPPP have had to struggle for support and they have no assurance of completion of their efforts. Unlike governments and traditional private industry, however, they can work with uncertain funding, sequential grants, volunteers and donations until such time as they are ready for launch. Then, they hope that popular interest and the opportunity for realization of a true interplanetary cruise vehicle will be so strong that the naysayers will be suppressed in favour of the dreamers. □



A solar sail is a mirror that uses sunlight to obtain a propulsive thrust. As each photon bounces off the sail, the reversal of its momentum shows up as a reaction force perpendicular to the sail. To go inwards towards the Sun, the operator sets the sail to reflect sunlight along the sail's velocity vector (direction of motion) in its orbit around the Sun. The thrust is then opposed to the motion around the Sun and the sail slows down. Solar gravity then pulls the spacecraft inwards and the sail spirals in towards the Sun. The process is reversed to sail outwards to Mars, the asteroids and the outer planets. It is theoretically possible to build a sail so light that it would 'feel' no gravity from the Sun and go off in a straight line away from the Solar System.

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Retrovirus evolution

Retroviruses and transposable elements — which came first?

from D.J. Finnegan

THE idea that retroviruses evolved from transposable elements (or vice versa) receives strong support in a paper from Tadayoshi Shiba and Kaoru Saigo published in this week's issue of *Nature* (see p.119). They are able to show that virus-like particles in cells of *Drosophila melanogaster* both contain RNA with sequences homologous to those of the *copia* element — the transposable element found throughout the *Drosophila* genome — and are associated with a reverse-transcriptase-like activity which is characteristic of vertebrate retroviruses.

That there is an evolutionary link between a transposable element, able to rearrange sequences within genomes, and a retrovirus, able to rearrange sequences between genomes, reinforces the view that eukaryotic genomes are more fluid than was once supposed and that barriers preventing transfer of information between species may not be impenetrable.

Data indicating that *copia*-like transposable elements of *D. melanogaster* may be related to vertebrate retroviruses have been accumulating for some time¹⁻³. Similarities were first noticed when the DNA sequence organization of proviruses, the integrated DNA copies of retroviral RNA, was compared with those of *copia*-like elements. Both types of element end in direct repeat sequences a few hundred base pairs long, with a length and sequence specific to each class of provirus or transposable element. In proviruses these are known as 'long terminal repeats' (LTRs). At the extreme ends of each element are short inverted repeats about 10 base pairs long which, with the exception of the *mdg3* family of *copia*-like elements, occur at both ends of the long direct repeats. Each element is flanked by a direct repeat of a small number of base pairs, the length, but not the sequence, of which is characteristic of a particular element. These bases are found only once at the target site for insertion and appear to be duplicated during transposition of a *copia*-like element or integration of a provirus³⁻⁵.

The similarities between proviruses and *copia*-like elements are not just structural. Both are transcribed into long polyadenylated RNAs which are initiated in one terminal direct repeat and terminated in the other. In the case of proviruses, some of these transcripts are packaged as viral genomes while others are processed and translated into viral proteins.

After retroviral infection of a host cell,

viral RNAs are copied by reverse transcriptase into linear double-stranded DNAs with a LTR at each end. These are converted into circular molecules, including species with either one LTR or two LTRs in tandem^{6,7}. If *copia*-like elements are really related to retroviruses then it would be expected that the circular DNAs found in *Drosophila* will contain *copia* sequences. Confirmation came when Flavell and Ish Horowitz screened the circular DNA in *D. melanogaster* tissue culture cells⁸ and found that it did indeed include species with all the sequences from the body of a *copia* element and either one long direct repeat or two repeats in tandem.

Several proviral sequences are known to be important for transcription or reverse transcription of the viral genome. These are (1) a promoter, or 'Hogness box', sequence and a polyadenylation signal in each LTR; (2) a sequence adjacent to the left-hand LTR allowing binding of the

tRNA used to prime synthesis of the first DNA strand after infection; and (3) a pyrimidine-rich sequence adjacent to the right-hand LTR and believed to be required for synthesis of the second DNA strand⁷. The corresponding regions of several different *copia*-like elements have been examined and found to have sequences analogous to some or all of these⁹⁻¹¹.

No infectious retroviruses have been found in *Drosophila* although virus-like particles have been seen in *D. melanogaster* tissues and cells in culture. Heine *et al.*¹² were able to isolate small amounts of subcellular particles associated with high-molecular-weight RNA and reverse transcriptase activity from *D. melanogaster* tissue culture cells. In the work reported in this issue of *Nature* (p.119), Shiba and Saigo have pursued this line of research further and report finding virus-like particles (VLPs) containing *copia* RNA.

Shiba and Saigo purified VLPs from sonicated tissue culture cell nuclei. As with retrovirus particles, two classes of RNA were found: low-molecular-weight 4–6S RNAs and heterogeneous high-molecular-weight RNAs about 5 kilobases long. Included in the high-molecular-weight class were molecules containing *copia* sequences.

Retroviruses code for at least some of their coat proteins and one might wonder whether the same is true of *Drosophila* VLPs. Apparently it is. Shiba and Saigo found that VLP RNA stimulated *in vitro* synthesis of polypeptides, many of which reacted with anti-VLP antisera. Moreover, most of the coding capacity of the VLP RNA was due to *copia* sequences since prehybridization of the RNA with *copia* DNA almost completely abolished its template activity. Finally, Shiba and Saigo have preliminary evidence indicating that reverse transcriptase activity, one of the diagnostic features of retrovirus particles, co-purifies with VLPs. These results are all consistent with the notion that a substantial proportion of VLPs are *copia* particles and that they may provide the missing link between *copia*-like transposable elements and retroviruses.

There are some surprising features of these results. The VLPs were isolated from nuclei and must have been present in large numbers (I estimate about 3,000 particles per cell based on the reported yield of 250 µg of VLP RNA per 1.5×10^{10} cells). This is unexpected since retrovirus particles and virus-like particles in vertebrate cells are assembled in the cytoplasm. Second, Shiba and Saigo were unable to detect homology between VLP RNA and DNA of members of three other families of *copia*-like elements — 297, 412 and 17.6. One might have expected sequences complementary to these transposable elements to have been found in VLP RNA since they have more structural similarities with proviruses than do *copia* elements. Shiba and Saigo do not indicate whether or not 297, 412 and 17.6

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RNAs were present in their cells and it is possible that these sequences were not being expressed.

Preliminary experiments indicated that VLPs are not infectious to *D. melanogaster* tissue culture cells. In this they more closely resemble the intracisternal A-type particles (IAPs) of mouse cells¹³ than infectious retrovirus particles. The similarity between VLPs of *D. melanogaster* and IAPs of *Mus musculus* is quite striking. They are both non-infectious virus-like particles containing long polyadenylated RNAs apparently coding for major components of the particles themselves¹⁴. In each case RNA in the particles is complementary to repeated DNA sequences. Sequences complementary to IAP RNA are repeated about 1,000 times and comprise about 0.3 per cent of the mouse genome¹⁵⁻¹⁷. *Copia* DNA sequences are only repeated about 100-200 times in the DNA of *D. melanogaster* tissue culture cells although, in total, *copia*-like elements constitute about 5 per cent of the genome^{5,18}.

Copia elements and DNA sequences complementary to IAP RNA are both transposable and can cause mutations by inserting into or adjacent to genes¹⁹⁻²². Their mechanism of transposition is unknown but in neither case can it involve extracellular virions. It could require reverse transcription of an RNA intermediate since preliminary results indicate that VLPs are associated with reverse transcriptase and the same may be true of IAPs²³. Alternatively, transposition may occur directly from DNA to DNA.

Temin has cogently argued that retroviruses evolve from transposable elements²⁴ but it is impossible to say at this stage whether *copia*-like elements and DNA complementary to IAP RNA are, or have been, evolving towards retroviruses or are descended from them. IAP RNAs are related to endogenous retroviruses in the Asian murine species *Mus cervicolor* and *Mus caroli*^{25,26}. Another possible link in the chain are the 30S RNAs found in mouse and rat cells in culture^{27,28}. Mouse 30S RNA is not normally found in either intracellular or extracellular particles but can be packaged by helper-independent type C viruses. This RNA, like IAP RNA, is complementary to DNA sequences bounded by direct repeats but it is not known whether or not these are transposable²⁹.

Rat 30S RNA has been implicated in retrovirus evolution since conversion of Moloney leukaemia virus to Harvey sarcoma virus and conversion of Kirsten murine erythroblastosis virus to Kirsten sarcoma virus appear to have resulted from incorporation of rat 30S RNA sequences by these viruses after growth in rat cells^{28,30}. □

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Cell motility

Brush borders on the move

from Harriet Harris

A GOOD model system for studying cellular mechanisms of movement should ideally fulfill three requirements. First, the components of the motile apparatus should be sufficiently ordered for the ultrastructure to be defined. Second, the system should be amenable to biochemical analysis. Last, but by no means least, the model must be seen to move in experimental conditions. Without this last property, the questions of how it works and even what it does can be answered only in a speculative fashion. One system that has been particularly thoroughly characterized, both structurally and biochemically, is the brush border of the intestinal epithelium. It is composed of numerous microvilli, which project into the intestinal lumen, together with an underlying network of cytoplasmic filaments, the terminal web. Each microvillus contains a bundle of microfilaments. Several proteins frequently associated with contractile arrays of actin, notably myosin^{1,2}, α -actinin³ and tropomyosin², are specifically excluded from the microvilli, but concentrated at the level of the terminal web. This latter structure thus appears, on biochemical evidence, to be poised for contraction, but what would be the nature of the resultant movement?

Experiments which appeared to show calcium- and ATP-dependent retraction of the microfilament bundles in the microvilli gave rise to attractive models for sliding filament interactions between the core bundles and terminal web myosin^{2,4,5}. Recently, however, the supposed 'retraction' was shown to be only the solvation of the microvillus cores at high Ca^{2+} concentrations⁶, through the action of the actin-severing protein, villin⁷. Thus, the brush border became a well defined structure of unknown functional capabilities. Now, however, two papers^{8,9} open the way to experimental analysis of brush border contraction and its regulation, by describing *in vitro* observations of movement.

Burgess⁸ and Keller and Mooseker⁹ have confirmed and extended the initial observation of Rodewald⁴ of an ATP-dependent contraction of the terminal web, perpendicular to the microvilli, which pinches in the edges of the cells. In Burgess' experiments, performed on sheets of whole glycerinated epithelial cells, contraction sometimes even tore the cells apart. Keller and Mooseker worked with sheets of brush borders, freed of cytoplasmic organelles. In both preparations it was evident that contraction pinched in the cells at the edges, at the level of the terminal web, while the microvilli concurrently fanned out, as if pulled together at the roots. There was no indication, in either system, that the

microvilli retracted. Both papers reported that contraction required ATP and was not supported by a non-hydrolysable analogue. One discrepancy between the papers was that the isolated brush borders were stimulated to contract by calcium, but the whole-cell preparations were not calcium sensitive. Since Ca^{2+} sensitivity is more easily lost than retained in non-muscle contractile systems¹⁰, it is likely that the isolated brush borders are more native in this respect. Ca^{2+} ions stimulated contraction at a 10-fold lower concentration than that required to solvate microvilli.

The roles of both myosin and Ca^{2+} in contraction were further clarified by biochemical tests⁹. In contraction conditions, micromolar concentrations of Ca^{2+} stimulated the phosphorylation of a single brush border polypeptide, the myosin 20,000-molecular weight light chain. The extent of phosphorylation correlated well with contractility. Furthermore, both Ca^{2+} -dependent contraction and phosphorylation were inhibited by trifluoperazine, a calmodulin-inhibiting drug. In platelets¹⁰ and thymus¹¹, Ca^{2+} -calmodulin activates myosin light-chain kinase and hence enhances myosin phosphorylation; this in turn stimulates both the actin-activated ATPase and myosin assembly into bipolar filaments¹². The behaviour of brush borders is thus entirely consistent with an actomyosin contraction, regulated by Ca^{2+} via a calmodulin-dependent myosin light-chain kinase.

To complete the picture, we need to know the ultrastructural organization of actin and myosin that leads to brush border contraction. One attractive hypothesis is

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Carboniferous fossils

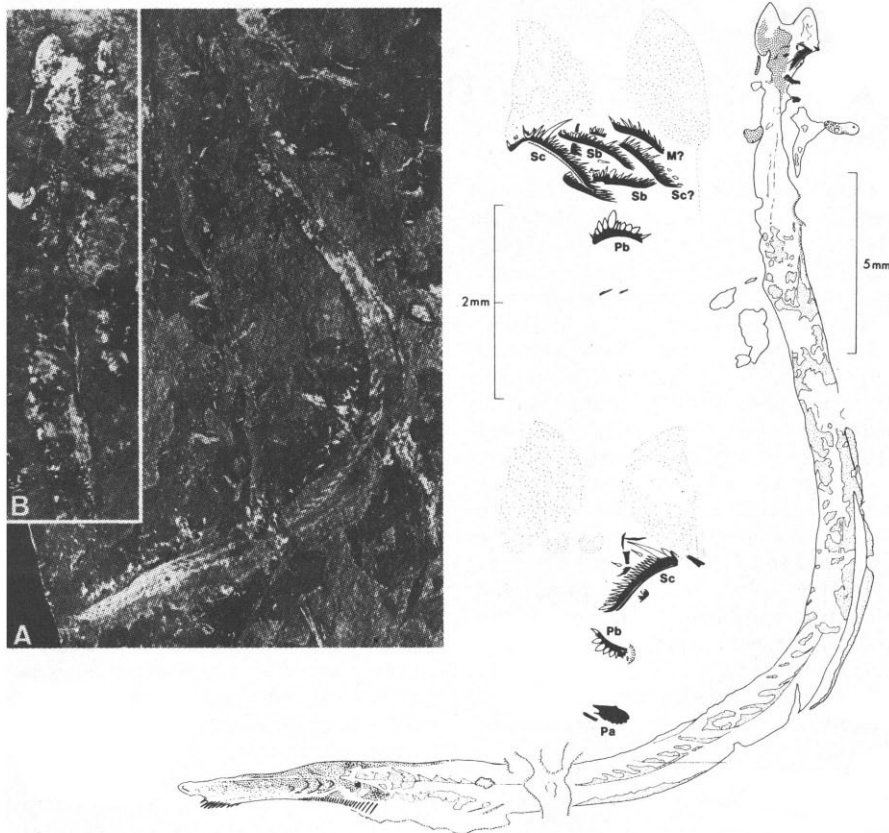
The conodont animal

from Alan Higgins

A unique fossil specimen containing a conodont apparatus has just been discovered in the Carboniferous of Scotland and reported in *Lethaia* (Briggs, D.E., Clarkson, E.N. & Aldridge, R.J. *Lethaia* 16, 1; 1983). The animal is about 4 cm long and has a slender eel-shaped body, as shown in the pictures on the right.

Conodonts are small — usually less than 1 mm — tooth-like phosphatic microfossils which occur in marine rocks of Cambrian to Triassic age. They have been studied intensely during the past 125 years, but their affinities have remained an enigma. As Müller (*Treatise of Invertebrate Paleontology*, 1981) noted, "the origin of conodonts is considered by many paleontologists to be one of the most fundamental unanswered questions in systematic paleontology".

Although normally conodonts are extracted from rock by acid digestion and are studied as single specimens, occasional finds of assemblages clearly indicate that conodonts occurred in the animal as an apparatus consisting of a large number of specimens, usually of differing structure. These discoveries, together with study of the conodont structure and distribution, have led to much speculation concerning their origin and they have been variously interpreted as the remains of plants, copulatory structures of nematodes, annelid jaws, vertebrate teeth and radulae of molluscs. In addition, recently two body fossils have been found in association with probable or confirmed conodonts. One, from the Carboniferous Bear Gulch Limestone of Montana, was a soft-bodied probable early vertebrate where the conodonts were preserved in the gut region; it is generally agreed that these were the remains of an animal eaten by the early vertebrate. The other, a unique specimen from the Burgess Shale, was interpreted as



A and B show the fossil as found in the Lower Carboniferous Granton Sandstones at Granton, Edinburgh: A, the conodont animal (head at the top); B, head and anterior trunk. The camera lucida drawings on the right are of the whole conodont animal and of the conodont assemblages.

a conodont animal but the tooth-like objects taken to represent the conodonts are so poorly preserved that this contender must be regarded as dubious.

The specimen described in *Lethaia* is convincing and has a body shape which is interpreted as being flattened in life with fins in the posterior part of the trunk. There is evidence of segmentation of the body and there are two faint axial structures in the anterior part of the trunk whose function is unknown. The conodonts occur as an assemblage of several specimens, whose structure and orientation would fit with known assemblages, in the head region of

the animal. Their function is still unknown but the authors are more inclined towards the teeth hypothesis than the tentacle supporting hypothesis which had previously been suggested.

The affinities of the animal, too, are unknown. Briggs, Clarkson and Aldridge considered seriously two possibilities — the chordates and the chaetognaths — but both were rejected and the animal referred to the Phylum Conodonta until further evidence of the soft parts is available. □

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that force is generated in a bundle of microfilaments which surrounds the terminal web at the level of the zonula adherens (part of the junctional complex between cells)^{8,13}. Radial contraction of this bundle, analogous to contraction in the cleavage furrow of dividing cells, would indeed constrict the apical region of the cell, causing the edges to pinch in and microvilli to fan out, as observed. Caution should be exercised in adopting simple models for brush border motility, however. The terminal web is a highly complex structure and contains a quantity of myosin which is not associated with the circumferential bundle of filaments. The microfilament bundles which extend from

the microvilli as compact 'rootlets' are linked to each other and to the underlying mesh of intermediate filaments by fine fibrils. Myosin is located around the rootlets¹⁴ and is likely to be a component of some of the fibrils¹⁵. At present it is not clear whether this myosin has a contractile or a structural function, and the possibility that it contributes to brush border contraction cannot be excluded. Much more detailed information is required on the location and state of assembly of myosin and the other components of this region of the cytoplasm.

One further question concerns the function of brush border contraction *in vivo*. The contractions observed with

glycerinated cells⁸ and isolated brush borders⁹ have abnormal characteristics: they are irreversible and they tend to pull cells apart. These may, however, be *in vitro* manifestations of a phenomenon which appears differently *in vivo*; local cycles of contraction, for example, might wave the microvilli about. Alternatively, the function of the actomyosin interaction in this instance may be to prevent rather than to produce movement¹⁶, exerting an isometric tension which maintains microvilli in an upright position. □

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Evolution and classification

Cladistics evolving gradually

from M. Howgate

THE British Museum (Natural History) may have relented and blunted the accent placed on cladistics in their public displays but the controversy still rages unabated. Well over 200 participants attended a recent seminar* in which the Museum's cladists, transformed and untransformed, defended their classificatory method and its implications for evolution. As with many such well orchestrated confrontations, the already well known positions were taken up, the current state of the art explained and little was resolved in the end; although the book *Evolutionary Cladistics* (by C. Hill and R. Fortey, British Museum, Natural History), an attempt to integrate 'woolly' evolutionary theory and 'strict' cladistic taxonomy, may herald a reconciliation of sorts.

Surprisingly, the meeting opened with a blistering attack (B. Halstead, Reading

University) on the transformation of the classical cladistics of Willi Hennig into what was dubbed 'natural order systematics'. This transformed what was a useful tool in phylogenetic reconstruction into a 'methodology raised up in its own right without any need of process, that is, evolution'.

While evolutionary systematics regarded species as more or less arbitrary subdivisions of a continuum, cladistics saw its role as the placing of taxonomy on a more objective plane. In particular, it attempts to set up refutable — in the popperian sense — hypotheses based on alternative cladograms (competing hypotheses of relationships) which map out nesting sets of shared derived characters — in Hennigese 'synapomorphies'. However, as Halstead pointed out, not only does cladistics replace putative ancestor-descendant relationships with purely nearest-neighbour relationships on a dichotomously branching cladogram, but transformed cladistics regards the evolutionary

'hypothesis' as a positive hindrance: "In Hennig's book, as in all early work in cladistics the nodes are taken to represent ancestral species. This assumption has been found to be unnecessary, even misleading, and may be dropped" (C. Patterson *The Biologist* 27, 234; 1980).

The cladistic system also denies the 'reality' of ancestral groups, continued Halstead, as they can only be defined by their possession of shared primitive characters (symplesiomorphies). Thus groups such as fish, amphibians and reptiles by definition would be 'unreal' groups in a cladistic taxonomy as they represented grades and not true clades, being defined only by the absence of advanced characters present in derived groups.

The problem was, contended Halstead, one of 'confused cladistics' in which species erected on evolutionary criteria were then used inappropriately to construct cladograms. With reference to the 'Man's place in evolution' exhibition at the Museum, he explained that cladograms give the impression of a hominid lineage made up of distinct branches when in fact we are viewing a single evolving lineage from *Homo habilis* to *H. erectus* and *H. sapiens* with the *Petalona* skull nicely spanning the divide between the latter species. A strict cladist should, of course, lump all this evolving lineage together into one species, since the last splitting event took place at the australopithecine level, a procedure which unfortunately results in a dramatic reduction in the amount of information contained in the classification.

C. Patterson (British Museum, Natural History), for the cladists, declined to be drawn into the controversy and instead pointed out the numerous contradictions between the evolutionary trees and tabulated classifications proposed by various evolutionary taxonomists. These, he said, stemmed mainly from undue weight being given to divergent lineages — a point which led him to his main endeavour: to explain the two possible ways in which a cladogram could be turned into an evolutionary tree. Either the cladogram must define the classification or else the classification must disregard some of the nodes of the cladogram. The problem with the former method — strict cladistics — is to develop a taxonomy with enough rank to accommodate a hierarchy which needs a separate rank name for each splitting event. Hennig himself needed to resort to a numerical method as the insects alone demanded over one hundred rank subdivisions. More recent workers (Rosen, for example), who adopt the same approach, end up with a plethora of new regimental taxonomic units — legions, cohorts, tribes and so on.

Patterson opts for the latter approach and circumvents the problem by introducing a series of conventions which in effect 'weight' the splitting events on a cladogram into those which give rise to new taxa and those, termed plesions, which are lumped

*'Cladistics and Classification', a review seminar organized by the Palaeontological Association, was held at Birmingham University on the 16 February 1983.

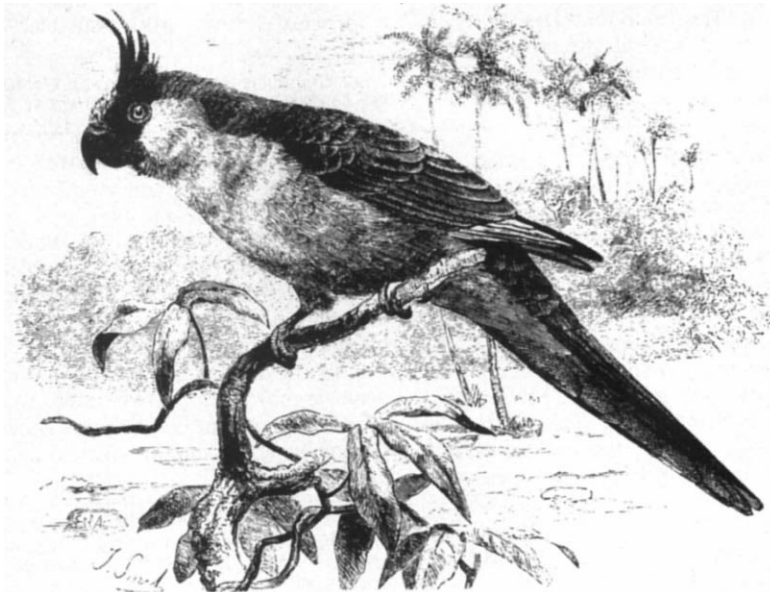
100 years ago

NEW OR RARE ANIMALS IN THE ZOOLOGICAL SOCIETY'S LIVING COLLECTION

THE UVAEAN PARRAKEET (*Nymphicus uvaensis*). In the second volume of Capt. Cook's "Voyage towards the South Pole and round the World" will be found (at p.110) a large, double, copper-plate engraving entitled a "View in the Island of New Caledonia," taken from a sketch prepared by Hodges, the artist of the expedition. The left-hand corner of this engraving contains a rude figure of a parrot with two feathers projecting from the summit of its head. This is doubtless the first representation ever given of the celebrated "Horned Parrot" of New Caledonia.

It would appear that the Uvaean Parrakeet, of which we now give an illustration (Fig.31), taken from one of the Zoological Society's living specimens, is a kind of satellite of the New Caledonian Parrakeet, as is the small island of Uvéa, in which it is found, of the larger island of New Caledonia. The small island of Uvéa, one of the Loyalty group, to which the new species is confined, consists, as Mr. Layard tells us, of a series of small islets joined together by a connecting reef with a lagoon in the centre. It is very singular that this distinct form should be found only in so restricted a locality, while its near relative, the "Horned Parrot" of Cook, appears to be distributed all over the large island of New Caledonia.

From *Nature* 27, 1 March 1883.



into plesiomorphic sister groups at the same taxonomic level. Thus while recognizing the difference between 'stem groups' of plesions and diversified 'crown groups' which are amenable to strict cladistic analysis, he insists that he avoids both the selection of arbitrary characters as the diagnostic criteria for higher taxonomic groups, such as the dentary/squamosal joint in defining mammals, and giving a high taxonomic rank to divergent lineages. Aves and Crocodilia, for example, should have the same rank despite the much greater diversity of the birds.

Cladistic classifications can be tested scientifically (C. Hill, British Museum, Natural History) by making retrodictions against the stratigraphical sequence of fossil forms and accepting ancestry in general, rather than postulating specific ancestors. This combination of cladogram and stratigraphy can be viewed as a mutual checking device in "the construction of absolute and correct evolutionary trees" (R.

Forley, British Museum, Natural History). But while genealogical history can be accepted as knowable, 'evolution via natural selection' remains hypothetical. Forley was even reconciled to accepting paraphyletic groups (groups defined only by the possession of shared primitive features) as 'real', so long as the taxonomic boundary was pushed far enough back to produce a monophyletic lineage, until he was asked where he would draw the line at the base of the reptilia. In discussion, Halstead was congratulated by A. Charig (British Museum, Natural History) for initiating a debate which resulted in the scientific staff of the Museum being brought back into consultation about museum display policy and it was pointed out that while for Hennig 'phylogeny was everything', for the transformed cladists 'phylogeny is nothing'. □

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Earth science

Why does a sedimentary basin subside — a model under test?

from R. McQuillin

In the recently published second edition of his book *The Interior of the Earth*¹, Martin Bott describes sedimentary basins of the continental interior as being subsidence features akin to those that occur at passive margins. How such basins develop is, in his opinion, still a matter of controversy. Modern ideas can be traced back principally to Sleep² in 1971 and Sleep and Snell³ in 1975 who provided a mathematical model describing the subsidence of passive margins and intra-continental basins in terms of thermal contraction in the lithosphere. They tested their model by comparing it with the observed subsidence history of the Atlantic coast of the United States of America and with subsidence of the Michigan Basin. When applied to such regions as the North Sea, the Sleep and Snell hypothesis encounters several problems; mainly those of space to accommodate the great volume of accumulated sediments in, for example, the Central Graben, and that of defining a plausible mechanism for the local heating of the continental lithosphere.

Dan McKenzie⁴ in 1978 observed that the history of development of the North Sea grabens (as well as that of other similar basins) was usually initiated by a period of subsidence associated with normal faulting, this being followed by regional subsidence which is only to a minor extent associated with faulting^{5,6}. It is this second phase of subsidence which can be modelled along the lines proposed by Sleep and Snell. McKenzie went on to propose that both space and heating problems could be

solved if a mechanism of crustal stretching is invoked. Mathematical treatment of this model is in terms of an instantaneous crustal extension followed by a period of thermal subsidence. The amount of extension is described by a factor β ; 'at time $t=0$ a unit length of continental lithosphere is suddenly extended to a length β , causing upswelling of hot asthenosphere'. His model predicts the amount of initial subsidence due to extension, the subsidence path following extension and the amount of crustal thinning. Thus the model can be tested by experimental determination of the degree of crustal thinning beneath a selected basin and comparison of the value so obtained with that which can be deduced from a plot of basin subsidence against time. Such a plot, which describes the subsidence path in the basin, can be derived from an analysis of well records (geological and geophysical), but in so doing it is necessary to adjust the observed time of deposition against present depth below sea-level curve for the effects of sediment loading and decompaction — effects which are superimposed on the loading induced by lithospheric cooling.

An early attempt to test the McKenzie hypothesis in the North Sea area⁷ was unfortunate in choice of location. A seismic refraction experiment was conducted across the Buchan and Witchground Graben; the degree of crustal thinning was determined and results were compared with data from five oil wells. However, the profile crosses a complex area where the Central Graben and Outer Moray Firth

Basin meet, and the conclusion that the area had been subject to an extension of between 50 and 100 per cent raised serious geological objections⁸.

A much more satisfactory attempt to test how well the uniform extensional model can explain the observed geological structure of a North Sea graben is now reported in this issue of *Nature* by Wood and Barton⁹. Results of a seismic refraction experiment show conclusive evidence for in excess of 10 km crustal thinning beneath the Central Graben, confirming a previous interpretation of gravity data¹⁰. What is of particular interest, however, is that β values estimated from well data do not fit those estimated from a simple model of a single extensional event to produce the present observed thinning. This disparity is interpreted as indicating that there has been a stretching event in the graben which predates the late Jurassic event which controls post-tectonic subsidence. Such an interpretation also avoids the difficulty of accommodating large block movements between and around the graben margins.

In the zone of major thinning under the graben, β values for the Jurassic extension lie between 1.35 and 1.55 so that only 30–50 km of extension is required, a result which more closely fits the predictions derived from other geological¹¹ and geophysical¹⁰ evidence than McKenzie's original prediction of 50–100 km. If an earlier phase of extension has affected the graben, when did this occur? It is tempting to suggest that this may correlate with the Permo-Triassic event proposed by Brumet and Le Pichon¹² to explain subsidence in the Paris Basin.

Having established that in broad terms, the McKenzie model explains the pattern of evolution of the Central Graben, can the same model be used to explain the evolution of other Mesozoic basins in the North-West European Continental Shelf? From gravity¹⁰ and seismic¹³ and structural¹⁴ evidence, it would appear that the Viking Graben formed as part of the same extensional event as the Central Graben. The Moray Firth Basin, however, appears to have formed by extension in the absence of

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substantial crustal thinning or post-tectonic subsidence¹⁴. Similarly, the massive accumulation of Jurassic and older sediments in the St George's Channel Basin followed by uplift, such that the Cretaceous is absent, then a phase of Tertiary subsidence, is indicative of a history which relates to a totally different causal mechanism.

One important line of investigation which has yet to be extensively applied in the study of extensional basins is that of deep reflection seismic profiling. In 1983 the British Institutions' Reflection Profil-

ing Syndicate (BIRPS) will study both areas in the North Sea and offshore south-west Britain. Data acquired during those experiments should provide crucial evidence on depth variation of the Moho associated with basin development and on the nature of faults deep in the crust where transition is expected to occur from brittle fracture to ductile flow during extension. □

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Translation control

Protein phosphorylation and translation of messenger RNAs

from Mike Clemens

It has been known for many years that parts of the complicated cellular machinery that translate messenger RNAs into proteins can be modified by reversible phosphorylation — the initiation factor eIF-2 (responsible for placing the initiating methionyl-tRNA on the ribosome) and the protein S6 (a component of the smaller ribosomal subunit) are the best studied examples. Now, it has been suggested that a third class of proteins involved in translation, the aminoacyl-tRNA synthetases, is subject to a phosphorylation-dephosphorylation process¹.

The aminoacyl-tRNA synthetases attach amino acids to tRNA during translation. Damuni *et al.*¹ have recently shown that, in extracts of rat liver, several aminoacyl-tRNA synthetases can be inactivated by incubation with ATP, provided that care is taken to inhibit protein phosphatase activity with sodium fluoride. A crude fraction containing the activity responsible for this effect (a putative protein kinase) was identified, as well as another fraction which reversed the inactivation and is presumed to contain one or more protein phosphatases. The effects of the fraction could be mimicked by addition of highly purified protein phosphatases from skeletal muscle or liver. Although no direct evidence for changes in the phosphorylation state of the various aminoacyl-tRNA synthetases has yet been obtained, the results clearly suggest that the enzymes can be regulated by such a mechanism. The major questions are, what factors may control the phosphorylation-dephosphorylation system and what is its physiological relevance?

According to Damuni *et al.*, both nutritional and hormonal control of aminoacyl-tRNA synthetase activity may occur by the reversible phosphorylation of the enzymes. Overnight starvation of rats led to a 50–60 per cent inhibition of at least five different synthetases and inhibition could be reversed by incubating the enzyme with the reactivating (protein phosphatase) frac-

tion. Exposure of isolated hepatocytes to the hormone glucagon together with a cyclic AMP phosphodiesterase inhibitor similarly inactivated the synthetases; insulin treatment of cells from starved rats produced the opposite effect.

The question of the physiological relevance of these changes poses more of a problem. First, modulation of rates of amino acid-charging on tRNA might be expected to affect the rates at which growing protein chains are elongated (since the charged tRNAs are the precursors for that process). Most evidence indicates, however, that it is the rate of ribosome attachment to mRNAs (initiation) rather than the rate of charging which controls the overall protein synthesis rate. Second, neither overnight starvation nor acute insulin administration has much effect on the rate of protein synthesis in liver *in vivo* (as opposed to the situation in skeletal muscle where protein synthesis is sensitive to such treatment). In experiments where precursor-specific radioactivity has been rigorously controlled and measured, no decreases in the rate of hepatic protein synthesis per ribosome have been seen in up to two days of starvation^{2,3}, although there was a small decline in ribosome number. Experimentally induced diabetes has been shown by McNurlan and Garlick⁴ to cause a 28 per cent fall in protein synthesis rate per ribosome *in vivo*; in perfused liver a larger effect was observed, although it was not associated with any lowering of the polypeptide chain elongation rate⁵. Insulin treatment only appears to reverse the inhibition of protein synthesis relatively slowly in the liver (requiring 24 h or longer). Clearly, these observations leave open the question of the role of the three- to four-fold changes in aminoacyl-tRNA synthetase activities obtained within 30 min in hepatocytes by Damuni *et al.*

It is possible that the regulation of translation in liver is different from that in skeletal muscle as the latter tissue is clearly

more sensitive to physiological changes. Recent work⁶ carried out at the University of Sussex suggests that starvation, diabetes and insulin treatment have substantial effects on the levels of initiation complexes formed between methionyl-tRNA and 40S ribosomal subunits. The changes are of the same magnitude as those seen in the rate of protein synthesis in muscle in these conditions. It seems difficult to link the regulation of initiation of translation to possible modulation of charging of tRNAs with amino acids, even if such a process also occurs in muscle. Nevertheless it is tempting to speculate on a possible relationship between aminoacyl-tRNA synthetase activity and polypeptide chain initiation.

It is well established that the availability of essential amino acids controls protein synthesis in cultured tumour cells and in normal tissues. Regulation occurs through modulation of initiation and involves a change in the activity of initiation factor eIF-2 (ref.7). Several pieces of evidence suggest that this regulation is not mediated directly by changes in tRNA charging levels, and yet recent studies⁸ at St George's Hospital Medical School on Chinese hamster ovary cell mutants containing a temperature-sensitive aminoacyl-tRNA synthetase show that initiation is controlled at the non-permissive temperature in a manner which is indistinguishable from the effects of amino acid starvation. Is there a regulatory function attributable to aminoacyl-tRNA synthetases, perhaps not directly involving tRNAs themselves? It may be relevant that many of the synthetases exist in the form of a high-molecular-weight multi-enzyme complex. Such a complex could include regulatory proteins, which might be the true substrates for the hormone-sensitive protein kinase(s) and phosphatase(s) studied by Damuni *et al.* Interestingly, the main effect of glucagon on protein synthesis in perfused liver is to prevent stimulation by added amino acids⁹.

Protein phosphorylation and translational control have proved uneasy partners in recent years. After eight years of investigation it is only now becoming apparent how eIF-2 activity may be controlled by phosphorylation, and the significance of the changes in the multiple phosphorylated forms of ribosomal protein S6 still has not been resolved. Let us hope that our understanding of the control of the aminoacyl-tRNA synthetases by protein kinases and phosphatases follows a smoother path. □

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Magnetic monopoles and the solar neutrino problem

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The suggestion that magnetic monopoles in the solar interior could affect the expected neutrino flux, thereby solving a longstanding problem in solar physics, is investigated. Bound states of particles in the region of a monopole are calculated using several simplifying assumptions, all of which can be expected to overestimate the effect of monopoles. It is found that the monopole density in the Sun would have to be 20 orders of magnitude larger than bounds set by the solar magnetic fields in order for there to be an appreciable effect on the solar neutrino problem.

WITH the announcement of a serious candidate for the detection of a magnetic monopole¹, attention has focused on possible ways in which the presence of grand unification theory (GUT) monopoles might affect physical processes. These objects, which are of a size comparable with other particles but possess masses of the order of 10^{16} GeV ($\sim 10^{-8}$ g), represent an entirely new form of matter^{2,3}, and a comprehensive phenomenology of their behaviour remains to be worked out.

If very massive monopoles exist, it is reasonable to suppose that gravitational interactions will cause them to congregate in regions of high matter density such as stars. Others^{4,5} have suggested that a collection of magnetic monopoles in a star such as the Sun could well catalyse the fusion reactions involving nuclei with magnetic moments which are attracted to the monopole by magnetic interactions. The end product is ${}^4\text{He}$ which, because it has zero magnetic moment, would not be bound, leaving the monopole free to initiate the process again. If such catalysis occurred, the expected solar neutrino flux from the Sun would be lowered because of two effects: (1) the solar temperature would be lower than is currently calculated on the basis of the assumption that fusion occurs through collision only, and (2) in addition, the reactions leading to the easily detected high-energy neutrinos would not be catalysed. Thus, there is the possibility that the existence of massive magnetic monopoles might have a role in the solar neutrino problem, one of the outstanding difficulties in physics and astronomy.

We now examine this possibility, concentrating on calculating the binding of ordinary particles to massive monopoles through the interaction of the particle magnetic moment with the monopole field. Because we are motivated by the possible connection of bound particle-monopole states to the solution of the solar neutrino puzzle, and because our conclusions are that monopoles cannot significantly alter the predicted neutrino flux by catalysing the fusion reactions in the Sun, we shall be concerned throughout with calculating the lowest reasonable bound states, rather than with calculating realistic binding energies. Our assertion is that if our calculation does not lead to any appreciable catalytic reaction in the Sun, then a more accurate calculation certainly will not do so.

Solar neutrino problem

The solar neutrino problem has been one of the most persistent astronomical problems of the past 15 years. The theoretically predicted fluxes [7.6 ± 3.3 SNU (3σ) = 10^{-36} captures s^{-1} per ${}^{37}\text{Cl}$ target atom (ref. 6)] have consistently been much larger than the experimentally measured⁷ value [2.1 ± 0.3 SNU (1σ)]. Virtually all forms of astronomical exotica have been considered (and rejected) as solutions. Superficially, at least, magnetic monopoles (GUTMM) offer another solution.

In a standard solar model the central temperature is $\sim 1.5 \times 10^7$ K so the typical thermal energy is 2 keV. A nucleon approaching another can only reach a distance of several hundred fermis before it is repulsed by the Coulomb force. For a nuclear reaction to take place the particle must tunnel through the rising barrier down to a distance of perhaps 1 fm where the nuclear forces take over. Folding the barrier penetration factor with the maxwellian distribution shows that most of the reacting particles have energies of many kT (10–30 keV) and must penetrate a barrier extending from tens of fm to 1 fm.

Now suppose a GUTMM was 'stuck' to a proton. At a distance of 1 fm the magnetic potential energy is ~ 30 MeV. Another properly oriented proton approaching this system would find the combined electric and magnetic fields to be attractive at distances closer than 40 fm. There the barrier penetration factor is radically altered. The rates would be so much larger than the standard p-p rate that the overall reaction rate would be determined more by the number of GUTMMs than temperature. Once the catalysed p-p reaction takes place the GUTMM would remain stuck to the deuteron. The ensuing ${}^2\text{H}(p, \gamma) {}^3\text{He}$ and ${}^3\text{He} ({}^3\text{He}, 2p) {}^4\text{He}$ reactions would similarly be catalysed. The GUTMM would be stuck on one of the final protons as ${}^4\text{He}$ has no magnetic moment. The ${}^3\text{He} ({}^4\text{He}, \gamma) {}^7\text{Be}$ reaction would not be magnetically catalysed. Because it leads to the easily detected neutrinos from ${}^7\text{Be} (e^-, \nu) {}^7\text{Li}$ and most importantly the ${}^8\text{B} (e^+, \nu) {}^8\text{Be}$ reactions, the neutrino flux from the Sun could be substantially reduced. The effectively increased cross-sections would also lead to lower temperatures and even fewer detectable neutrinos. (If the p-e-p reaction was catalysed by GUTMMs, however, the predicted detectable neutrino flux could actually increase.)

Binding of particles by monopoles

A magnetic monopole of strength g sets up a purely radial magnetic field whose strength at a distance r from the monopole is given by g/r^2 . A monopole, therefore, cannot exert a force on a stationary electrical charge, nor can it do work on a moving charge. On the other hand, every charged particle which exists in nature has, in addition to its charge, a magnetic moment. This moment will interact with the monopole field in the standard way, the force between the two being given by

$$F = \nabla(\boldsymbol{\mu} \cdot \mathbf{B})$$

where $\boldsymbol{\mu}$ is the dipole moment of the particle. The existence of this interaction introduces the possibility of a bound particle-monopole system.

Let us assume that the particle dipole moment is at all times aligned with the monopole field. This assumption results in a great simplification, and it is constant with our philosophy

outlined above. If we allowed the spin to be anti-aligned, then the states we calculate would have to be replaced by states which were linear combination of spin-aligned and spin-anti-aligned states. But as the anti-aligned states will have a much higher energy than the aligned states, such a mixture would necessarily have a higher energy than the ones we calculate. Thus, a more realistic calculation which included spin effects would not produce more binding than the calculation which results from this simplifying assumption. The potential in which the particle finds itself, then, is

$$V(r) = -\mu \cdot \frac{rg}{r^3} \quad (1)$$

This potential is well known to be pathological⁸, being plagued by the problem of 'fall to the centre', in which any particle in the potential will eventually fall to an energy state at minus infinity. This pathology only arises, however, if we assume that the equation (1) represents the particle-monopole potential all the way to $r=0$. There are, however, simple physical reasons to suppose that it does not.

The energy density of a magnetic field is just $B^2/8\pi$. This becomes infinite as we approach a point monopole. Suppose we ask the value of r at which the energy in a sphere whose radius is equal to the classical electron radius reaches twice the electron mass. At this distance from the monopole there is sufficient energy stored in the field to create an electron-positron pair.

A simple calculation shows that the critical distance, r_c , is given by

$$\frac{1}{8\pi} \frac{g^2}{r_c^4} \frac{4}{3} \pi \left(\frac{e^2}{mc^2} \right)^3 = 2mc^2$$

where m is the electron mass. This gives

$$r_c \approx 10^{-12} \text{ cm} = 10 \text{ fm} \quad (2)$$

We shall assume that the particle experiences a potential given by equation (1) for $r > r_c$. At radial distances less than this, we expect that pair production off of the static monopole field will produce a cloud of dipole-anti-dipole pairs. This sort of effect is well known for heavy nuclei, where pair creation off of the static electric field gives rise to 'sparking' in the vacuum⁹.

Although the actual behaviour of the potential for $r < r_c$ is complicated, clearly the classical description of a point monopole breaks down at this point. We shall just assume that $V(r) = V(r_c)$ in this region (that is, that the potential is given by equation (1) for large r and constant inside of the critical radius). It is unlikely that our conclusions will be affected by this simplification, and we shall perform a numerical investigation of the dependence of our results on the precise value of r_c .

Having defined our potential, we can now write the Schrödinger equation in the form

$$\left(\nabla^2 - \frac{2M}{\hbar^2} E - \frac{2M}{\hbar^2} V \right) \Psi = 0 \quad (3)$$

where

$$\begin{aligned} V(r) &= -g\mu/r^2 & r > r_c \\ V(r) &= -g\mu/r_c^2 & r < r_c \end{aligned}$$

and M is the mass of the particle being considered. Solutions were obtained by expanding in a power series at the origin and then integrating outwards by means of the Numerov method. A variable mesh was used to ensure accuracy.

Results for single particle states

We can write the magnetic moment of a particle of mass M and spin S in the form

$$|\mu| = Q \frac{e\hbar}{2Mc} S$$

where we have written Q instead of the customary spectroscopic g -factor to avoid confusion with the magnetic charge. In terms of this notation, the quantity $2M/\hbar^2 V$ which appears in

Table 1 Binding energies of ground states and first excited states

Particle	E_B (keV)	$r_{\max}$ (fm)	E_1 (keV)	$r_{\max}$ (fm)
e^-	67	211	2×10^{-3}	10^5
p	17	21	0.46	434
D	1.3	270	—	—
^3He	1.2	104	—	—

equation (3) takes on a particularly simple form:

$$\frac{2M}{\hbar^2} V = \frac{-2M}{\hbar^2} gQ \frac{e\hbar}{2Mc} \frac{1}{2} \frac{1}{r^2} = \frac{Q}{4r^2}$$

where we have used the Dirac¹⁰ quantization condition ($eg = \hbar c/2$) to get the second equality. This expression is completely independent of the mass, so that from the form of the Schrödinger equation we would expect the product of the mass times the binding energy to be constant. This conclusion would be rigorously true if Q were the same for all particles, and we do find this scaling when we compare the binding energies of the electron with a 'proton' that has no anomalous magnetic moment. It turns out, however, that the binding energy is very sensitive to the actual value of Q , so that the results for real particles will not display this scaling, although we will see that more massive particles do tend to be less tightly bound than less massive ones.

Note, however, that our ordinary intuition about bound states, in which higher binding energies correspond to smaller orbits, need not apply in this case. Because the magnetic moments of different particles are different, each particle in a bound state near a monopole sees a different potential. The only thing that all the potentials have in common is the cutoff in equation (2), as this value was arrived at by a process independent of the particle being bound.

With this important point in mind, we can consider the numerical results derived from equation (3) for electrons, protons, deuterons and ^3He . In all that follows we choose the Dirac value of the magnetic charge¹⁰, which means that we take $g = 3.3 \times 10^{-8}$ e.s.u. In Table 1 we list the binding energies of the ground states, the point at radius at which the ground state wave function reaches its maximum value, and the same quantities for some first excited states. Except for the electron we did not search for states having binding energies below a few hundred electron volts, because such states would surely not be heavily populated in the solar interior.

From our arguments on the dependence of binding energy on mass, we expect heavier nuclei to be bound with energies of < 1 keV.

Note here that the fact that we have ignored spin orientation effects in this calculation means that the energies in Table 1 must be considered as lower bounds on the true binding energies. In fact, some authors have argued^{11,12} that including these effects will result in a situation where the electron has no bound states at all, although these conclusions would not necessarily apply to particles like the proton which have large anomalous magnetic moments.

Results for multiparticle states

To discuss catalysis, we need to know what happens when more than one particle is bound to the same monopole. The correct way to handle this problem would be to do a complete self-consistent calculation, which is not a trivial undertaking. We have elected to use the following approximation to a self-consistent calculation: if a particle of charge Z_1 is already bound to a monopole, then for purposes of considering the binding of the next particle of charge Z_2 , we will treat the charge Z_1 as if it were located at the origin. Thus the second particle will see a potential

$$V = \frac{-\mu g}{r^2} + \frac{Z_1 Z_2}{r} \quad (4)$$

instead of that given in equation (1).

This scheme can be expected to work best when the first particle bound to the monopole is localized at a relatively small radius, so that we can replace it with a point charge at the origin. If this condition is not met, then this procedure would greatly overestimate the effect of electrical charge, because only that part of the charge cloud of the first particle which lies within the orbit of the second can contribute to the binding.

Let us begin our analysis of the possibility of a catalytic reaction by looking at positively charged particles bound to a monopole. The average Boltzmann energy in the solar core is a few keV, so even if a deuteron or ^3He were to be bound, Table 1 shows that their binding energies are too small to allow them to remain with the monopole long enough for another capture to occur. Therefore, the only possible scenario is one in which the proton is bound to the monopole first. Because the classical radius of the proton orbit is considerably smaller than any of the other orbits associated with positive charges in Table 1, our approximation scheme should work in this case. Using the potential in equation (4) and the numerical scheme discussed above for a second positively charged particle encountering a monopole-proton system, we find that the second particle must be unbound. In other words, the Coulomb repulsion in this case is enough to prevent the second particle from being trapped by the monopole. Thus, once a monopole has acquired a net positive charge, no further positive particles can be bound to it. Indeed, given the rather weak binding of particles in the monopole potential, it is not too surprising that adding a small repulsive force can completely eliminate bound state solutions from the problem. We conclude, therefore, that no catalysis can occur through a process in which two positive charges are attached to a single monopole.

The only way left for the monopole to initiate catalysis, then, is for it to bind an electron first, thereby increasing the attractive nature of the potential. Unfortunately, if we calculate the ground states of the proton, deuteron and ^3He using equation (4), we find that the predicted wave functions have their maxima well inside the orbit of the electron ground state given in Table 1, so that our approximation scheme will not work. We can, however, argue that if the electron is to provide extra binding for positive particles, then the orbits of these particles are likely to lie outside the orbit of the electron. This, in turn, means that even in this most favourable case, we can expect the separation of the positive particles around a monopole to be of the order of 50–100 fm.

Consequence for solar neutrinos

We recognize three mechanisms by which the binding of particles to monopoles could resolve the solar neutrino difficulty: (1) shunting of reactions through non-neutrino producing branches by catalysing the ^3He – ^3He reaction; (2) increasing the p–p reaction so that the solar core temperature can be reduced; or (3) catalysing the e – ^7Be reaction so that the high-energy ^8B neutrino detected most readily by the ^{37}Cl experiment is not produced.

(1) ^3He – ^3He . An electron– ^3He bound state would have a net positive charge, so a second ^3He would not be bound. A second electron could not be in the same orbit as the first because of the Pauli principle, and the next excited state is so far from the monopole that it would have no effect on this conclusion.

(2) p–p. The second proton could not be in the same state as the first. Because the electrical charges of the electron and first proton cancel, our approximation scheme would predict the same binding energy for the second proton in this system as it would for the first excited state of a proton on a bare monopole.

First, the 0.46-keV binding energy makes it unlikely that this system would appear very often, as the second proton is susceptible to ionization through collisions. Second, if catalysis did occur, we would expect the p–e–p reaction to be catalysed together with the p–p. Because the former reaction produces a measurable neutrino which is not seen, it seems unlikely that the latter reaction will be enhanced.

Even if we ignore these two facts and assume that we have a stable two proton bound system, we encounter problems. The two protons typically find themselves ~ 100 fm apart and hence the monopole does not directly reduce the Coulomb barrier. It does, however, keep the protons in the same general vicinity and the inner proton might be thought of as approaching the edge of the barrier of the outer proton on each orbital period. The proton might thus approach the second at a rate of perhaps 10^7 higher than protons in the thermal plasma and the reaction rate may increase by the same factor. From ref. 6 we can estimate that the p–p rate must be increased by 30% to give an appropriate flux. This would require that roughly 1 proton in 10^8 be bound to a monopole or, if the monopoles are confined to the inner 10% of the Sun, then 10^{49} monopoles would be required. The mass of the Sun would come almost completely from monopoles. The number of monopoles is a factor of 10^{20} higher than that required to explain the apparent monopolar charge of the Sun. It is even more discrepant with numbers considered reasonable in refs. 4, 5. Even if the flux from ref. 1 is true and every monopole which ever hit the Sun was captured, the resulting number of monopoles falls 18 orders of magnitude too low to affect the p–p reaction significantly.

(3) From our discussion of the form of the Schrödinger equation and the dependence of the binding energy on mass, we would expect ^7Be to be bound to a bare monopole with 1 keV or less, so the system will be broken up by collisions in the solar core. The only way to catalyse the reaction, then, is to have the ^7Be and the electron bound to the same monopole. The reaction rate might then scale as the ratio of the electron density in the bound system to that in the plasma. The increase in reaction rate would be a factor of 10^7 or so, so we would need one monopole for every 10^8 electrons—a number which again exceeds reasonable limits on monopole density by roughly 20 orders of magnitude.

It is particularly difficult to think of ways to change the main thrust of these conclusions. We have investigated the dependence of our results on the numerical value of the cutoff parameter, for example, and we find that even taking the cutoff where the energy density of the magnetic field is a factor of 10 greater than the minimum needed for pair production, does not increase any of the crucial reaction rates sufficient to make a dent in the 20 orders of magnitude deficit we have found.

Conclusion

We conclude from these arguments that even if we put the most optimistic possible interpretation of the problem of the binding of particles to magnetic monopoles, the straightforward types of catalytic processes that might alleviate the solar neutrino problem simply will not work. Either the catalysis is much more subtle than what we have considered or it does not take place at all. Catalysis of fusion by magnetic monopoles appears to be another non-solution to the solar neutrino problem. We note, however, that this argument does not prove that there are not monopoles in the Sun—just that if they are there they do not affect the neutrino flux by means of a catalytic reaction.

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Molecular cloning and nucleotide sequence of a transforming gene detected by transfection of chicken B-cell lymphoma DNA

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A transforming gene detected by transfection of chicken B-cell lymphoma DNA has been isolated by molecular cloning. It is homologous to a conserved family of sequences present in normal chicken and human DNAs but is not related to transforming genes of acutely transforming retroviruses. The nucleotide sequence of the cloned transforming gene suggests that it encodes a protein that is partially homologous to the amino terminus of transferrin and related proteins although only about one tenth the size of transferrin.

A VARIETY of different types of neoplastic cells contain activated transforming genes which can be detected by their ability to efficiently transform NIH 3T3 mouse cells upon transfection (see ref. 1 for review). Examples of such neoplasms are chicken B cell lymphomas². These lymphomas are induced by infection with avian lymphoid leukemia virus (LLV), a retrovirus which induces neoplasms with long latent periods and does not contain a specific viral transforming gene. High molecular weight DNAs of these lymphomas transform NIH 3T3 cells with efficiencies of approximately 0.1 transformant per μg DNA². In contrast, DNAs of LLV-infected non-neoplastic tissues lack transforming activity, indicating that a transforming gene has been activated during the neoplastic process². Analysis of NIH cells transformed by LLV-induced B-cell lymphoma DNAs indicates that the activated transforming gene detected by transfection is not linked to viral DNA sequences².

In 80–90% of LLV-induced lymphomas, a second candidate transforming gene (*c-myc*) is activated as a consequence of adjacent integration of exogenous viral DNA³. Analysis of NIH cells transformed by lymphoma DNAs further indicates that the transforming gene detected by transfection is not homologous to *c-myc*, suggesting that at least two different candidate transforming genes are activated in these neoplasms⁴. Since lymphomagenesis seems to be a multi-step process⁵, it has been suggested that activation of these two genes may be involved in different stages of development of neoplasia⁴.

We report here the molecular cloning and characterization of the transforming gene detected by transfection of chicken B-cell lymphoma DNA. The isolated transforming gene is homologous to a family of sequences present in DNA of normal chicken cells. Homologous sequences are detected in human DNA, indicating that this gene family is well conserved in evolution. The nucleotide sequence of the transforming gene suggests that it encodes a small protein which shares homology with proteins of the transferrin family.

Molecular cloning of the transforming sequence

A biologically active transforming gene was cloned from NIH cells transformed by DNA of the established chicken lymphoma cell line RP9. DNA of these cells was partially digested with the four base-recognition restriction endonuclease *Mbo*I. DNA fragments of approximately 5–20 kilobases (kb) were purified by sucrose gradient centrifugation and ligated to *Bam*HI arms

of λ Charon 30⁶. The ligated DNA was packaged *in vitro*⁷ to generate a library of approximately 200,000 recombinant phage. This phage library was screened by sib-selection⁸ using transfection of NIH 3T3 cells as an assay to identify recombinant phage populations which contained an active transforming sequence.

The library was initially divided into 10 pools of 20,000 phage. Each pool was amplified in *Escherichia coli* strain LE 392 first as a plate lysate and then in liquid culture. DNA of each phage pool was then assayed by transfection of NIH 3T3 cells (Fig. 2 legend) and one pool which contained transforming DNA was identified. The original plate lysate of this pool was divided into 10 pools of 4,000 phage which were amplified and assayed as described above. Three of these phage pools contained transforming DNA and the original plate lysate of one

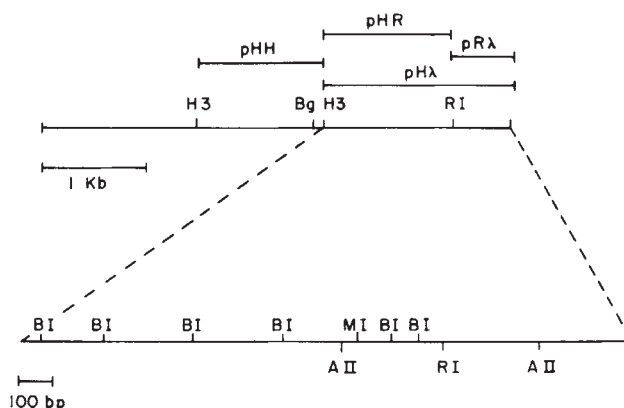


Fig. 1 Restriction map of the cellular insert of λ ChBlym-1. Recognition sites for the restriction endonucleases *Bgl*II (Bg), *Eco*RI (RI) and *Hind*III (H3) in the cellular insert of λ ChBlym-1 are shown (middle). The λ clone contains one of the two 7.5 kb internal *Bam*HI fragments of intact Charon 30 DNA to the right of the cell insert (not shown). The bars designated pHR, pRλ, pHH and pHλ (top) indicate the name and location of cellular DNA fragments of λ ChBlym-1 subcloned in pBR322. The plasmids pRλ and pHλ also contain 0.8 kb of λ DNA to the right of their cellular inserts and terminate at a *Hind*III site in λ DNA (not shown). A fine-structure map of the cellular insert of pHλ (bottom) indicates that it contains recognition sites for *Ava*II (AII), *Bst*NI (BI) and *Mnl*I (MI) in addition to *Eco*RI.

of these positive pools was divided into 50 pools of 250 phage. These pools were amplified and assayed by transfection, in this case with intact phage particles rather than with purified phage DNA (Fig. 2 legend). Two positive phage pools were identified and 360 individual phage plaques were picked from the plate lysate of one of these positive pools. These individual plaque harvests were pooled in groups of 20, amplified in liquid culture and assayed by transfection with phage particles. One positive pool was identified and the individual phage plaques which constituted this pool were separately amplified and assayed. A single positive phage plaque was identified and further plaque purified. This clone is designated λ ChBlym-1.

Structure and transforming activity of λ ChBlym-1

λ ChBlym-1 was characterized by cleavage with a series of restriction endonucleases. The clone contains a cellular insert of 4.5 kb which includes recognition sites for *Bgl*II, *Eco*RI and *Hind*III (Fig. 1). The transforming activity of λ ChBlym-1 corresponds to 100–500 transformants per μ g of total λ DNA (Fig. 2). Similar efficiencies of transformation were obtained with purified phage DNA and intact phage particles. Since the total phage DNA is approximately 44 kb, the transforming activity of λ ChBlym-1 corresponds to approximately $1\text{--}5 \times 10^5$ transformants per μ g of cellular DNA. This transforming activity is similar to those of previously described molecular clones of viral transforming genes and represents an enrichment of about 5×10^4 compared with the initial transforming activity of DNA of the transformed NIH cells from which the clone was isolated (0.05 transformant per μ g DNA).

To localize the transforming sequences, λ ChBlym-1 was digested either by *Hind*III alone or by *Hind*III plus *Eco*RI and four fragments containing cellular sequences were subcloned

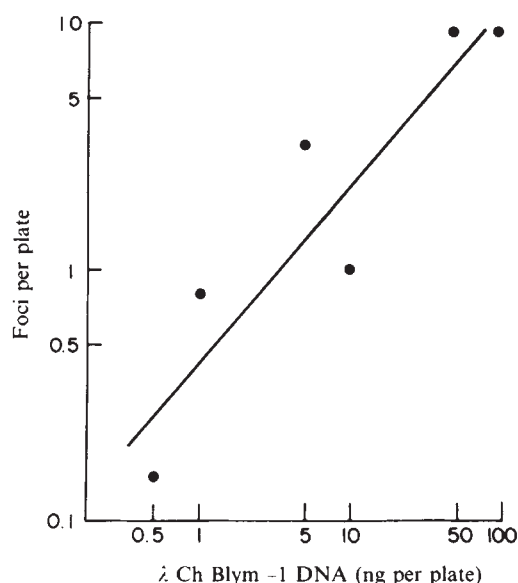


Fig. 2 Transforming activity of λ ChBlym-1. λ ChBlym-1 phage particles were collected by centrifugation from clarified liquid lysates of *E. coli* strain LE392, resuspended in 0.1 M NaCl, 0.01 M MgCl_2 , 0.02 M Tris-HCl (pH 7.5) and incubated for 30 min at 37 °C with RNase A ($100 \mu\text{g ml}^{-1}$) and DNase I ($10 \mu\text{g ml}^{-1}$). Phage were again pelleted and resuspended in the above buffer. DNA was either extracted from this phage preparation or the concentrated phage particles were used directly for transfection. Recipient cultures of NIH 3T3 cells were exposed to 10^7 , 10^8 or 10^9 phage particles (corresponding to 0.5, 5 or 50 ng of phage DNA) or to 1, 10 or 100 ng of purified phage DNA. Both phage particles and DNA were mixed with carrier NIH DNA (20 μ g per recipient culture) and assayed as previously described⁵³. Foci were counted 16 days after transfection and results are presented as the average number of foci from 4–6 recipient cultures exposed to each inoculum of phage particles or phage DNA. No foci were obtained on 4 recipient cultures exposed to NIH DNA alone.

Table 1 Transforming activity of λ ChBlym-1 DNA fragments

DNA	Foci per μ g cell DNA	DNA	Foci per μ g cell DNA
λ ChBlym-1	2×10^3	pR λ	<20
pH λ	5×10^3	pH λ <i>Bst</i> NI	<20
pHH	<20	pH λ <i>Ava</i> II	<20
pHR	<20	pH λ <i>Mnl</i> I	<20

Transforming activities of λ ChBlym-1 and plasmid subclone DNAs were assayed by transfection of NIH 3T3 cells. Plasmid DNAs were either linearized by digestion with *Bam*HI or were digested to completion with *Bst*NI, *Ava*II or *Mnl*I as indicated. At least twelve recipient cell cultures were exposed to 10–100 ng of cloned DNAs and 20 μ g of carrier NIH DNA per culture. Foci were counted 13–16 days after transfection and results are expressed as foci per μ g of cell insert DNA.

in pBR322 (Fig. 1). The plasmid designated pH λ was found to retain the transforming activity of the original λ clone (Table 1). This plasmid (Fig. 1) contains 1.8 kb of cellular sequences linked to 0.8 kb of phage DNA. In contrast, the plasmid designated pHH (Fig. 1) lacked transforming activity (Table 1). Double digestion by *Hind*III plus *Eco*RI cleaved the cellular DNA insert of pH λ to generate two plasmids designated pHR and pR λ (Fig. 1). These plasmids, which contain 1.25 and 0.55 kb of cellular sequences respectively, lack transforming activity (Table 1). Therefore, the transforming sequences of λ ChBlym-1 are contained within the 1.8 kb cellular DNA insert of pH λ and span the *Eco*RI site.

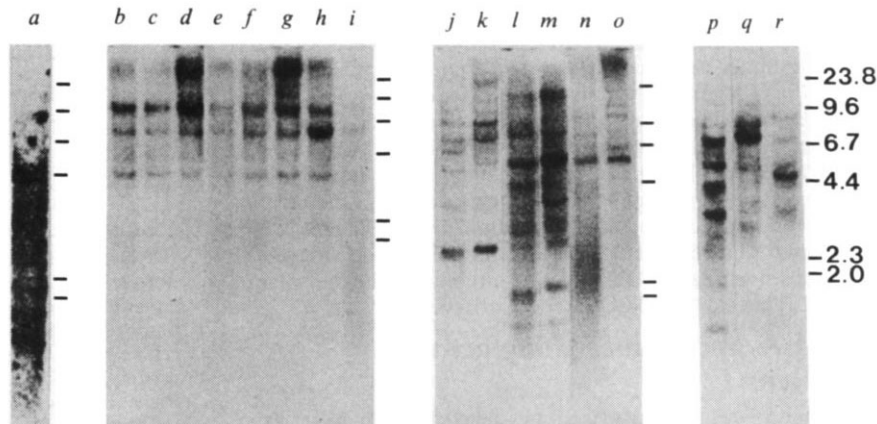
A fine-structure map of pH λ (Fig. 1) shows that the cellular insert also contains 6 *Bst*NI sites, 2 *Ava*II sites and 1 *Mnl*I site. It lacks recognition sites for *Acc*I, *Ava*I, *Bgl*I, *Bgl*II, *Bst*EII, *Hae*III, *Hgi*AI, *Kpn*I, *Mst*II, *Nae*I, *Nar*I, *Nru*I, *Pst*I, *Pvu*II, *Sac*I, *Sal*I, *Xba*I and *Xho*I. To further localize the transforming sequences, pH λ DNA was digested separately with *Ava*II, *Bst*NI and *Mnl*I and assayed by transfection. All of these enzymes abolished transforming activity (Table 1). These results indicate that the region of the clone between the two *Ava*II sites carries transforming sequences and that the transforming region spans at least one of these *Ava*II sites.

Homology of the transforming gene of λ ChBlym-1 to a conserved family of cellular DNA sequences

The organization of cellular DNA sequences homologous to the cloned transforming gene was investigated by Southern blot analysis⁹. Hybridization of ^{32}P -labelled pHR to chicken DNA detected highly repetitive sequences (Fig. 3, lane a), indicating that the region of the clone to the left of the *Eco*RI site contains repetitive chicken DNA. In contrast, a probe (M13R9) extending from the *Eco*RI site to 12 nucleotides past the right *Ava*II site hybridized to discrete fragments of chicken DNA (Fig. 3, lanes b–o). This probe detected four major bands (>30, 7.4, 6.0 and 3.7 kb) and several minor bands (6.6, 3.5 and 2.4 kb) in *Eco*RI digests of DNAs of RP9 cells, primary chicken B-cell lymphomas, and normal chicken cells (Fig. 3, lanes b–i). These results indicate that the transforming gene of λ ChBlym-1 is homologous to normal chicken DNA sequences and that these sequences are not amplified in lymphomas. The detection of multiple chicken DNA fragments homologous to the transforming sequence further indicates that this transforming gene is related to a small family of normal chicken genes, rather than to a single-copy gene.

To further investigate the organization of chicken DNA sequences homologous to the λ ChBlym-1 transforming gene, DNAs of normal and lymphoma cells were digested with a series of restriction endonucleases (*Bam*HI, *Bgl*II, *Hind*III, *Pvu*II, *Sac*I, *Xba*I and *Xho*I) which did not cleave within the transforming clone. Examples of *Bgl*II, *Pvu*II and *Xho*I digests of DNAs of RP9 lymphoma cells and normal chicken embryo fibroblasts are presented in Fig. 3, lanes j–o. In all cases, multiple

Fig. 3 Analysis of cellular DNA sequences homologous to λ ChBlym-1. *a*, *Hind*III-digested chicken DNA hybridized with pHR probe. *b-i*, *Eco*RI-digested chicken DNAs hybridized with M13R9 probe: *b*, lymphoma B7362; *c*, normal erythrocytes from bird 2993; *d*, lymphoma from bird 2993; *e*, normal kidney; *f*, lymphoma from bird 2902; *g*, normal erythrocytes from bird 2902; *h*, normal chicken embryo fibroblasts; *i*, RP9 lymphoma cell line. *j-o*, *Bgl*II- (*j* and *k*), *Pvu*II- (*l* and *m*) and *Xho*I-digested (*n* and *o*) DNAs of normal chicken embryo fibroblasts (*j*, *l* and *n*) and RP9 lymphoma cells (*k*, *m* and *o*) hybridized with M13R9. Lanes *p-r* are human DNAs digested with *Bam*HI (*p*), *Eco*RI (*q*) and *Hind*III (*r*) and hybridized with M13R9. The sizes of marker fragments of *Hind*III-digested λ DNA are indicated in kb.



Methods: Cellular DNAs (10 μ g) were digested with restriction endonucleases, electrophoresed in agarose gels and analysed by Southern⁹ blot hybridization. Filters were hybridized with $1.5\text{--}2.5 \times 10^5$ c.p.m. per ml of 32 P-DNA probe and washed as described by Hanahan and Meselson⁵⁴, except that 10% dextran sulphate was included in the hybridization buffer. Autoradiographic exposures were for 1–3 days. DNA of pHR was labelled by nick-translation⁵⁵. M13R9 probe was prepared from an M13 clone as described by Hu and Messing⁵⁶. This clone (see Fig. 4 legend) contains 252 nucleotides to the right of the *Eco*RI site.

fragments of chicken DNA homologous to the transforming sequences were detected. Most homologous fragments of normal and lymphoma DNAs co-migrated, although some differences between lymphoma and fibroblast DNAs were detected. It seems likely that these occasional differences are a consequence of genetic polymorphism rather than tumour-specific DNA rearrangements since (1) similar polymorphisms were detected in blot-hybridization analysis of normal cell DNAs of different inbred lines of chickens, and (2) DNAs of normal and lymphoma tissues of the same birds yielded the same pattern of fragments homologous to M13R9 (data not shown). However, due to the complexity of the sequence family homologous to the transforming gene, the possibility of tumour-specific DNA rearrangements cannot be excluded by this analysis.

To examine the evolutionary conservation of the transforming sequence, M13R9 probe was hybridized to Southern blots of human DNA. Multiple homologous fragments were detected in *Bam*HI-, *Eco*RI- and *Hind*III-digested human DNAs (Fig. 3, lanes *p-r*). Using hybridization and washing conditions of moderate stringency, similar intensities of hybridization to human and chicken DNAs were observed (Fig. 3), but the hybridization to human DNA was less intense using conditions of greater stringency. These results indicate that the gene family homologous to the λ ChBlym-1 transforming gene is well conserved in vertebrate evolution.

In contrast to the discrete DNA fragments detected in chicken and human DNAs, hybridization of M13R9 probe to mouse DNA revealed repeated sequences which appeared as an intense dispersed smear in blot hybridization analysis (not shown). The nucleotide sequence of this region of the transforming gene (see below) indicates that it contains 19 nucleotides (beginning 27 nucleotides to the right of the *Eco*RI site) which are 79% homologous to mouse satellite DNA¹⁰. Since mouse satellite DNA constitutes 8% of the mouse genome¹¹, this partial homology is likely to account for the detection of highly repeated mouse sequences with M13R9 probe. A second sequence of 18 nucleotides 70% homologous to mouse satellite DNA was also present (beginning 34 nucleotides to the left of the *Eco*RI site) and pHR probe also hybridized to highly repetitive mouse DNA sequences (not shown). Due to the presence of these sequences in the transforming region, it was not possible, using these probes, to analyse DNAs of normal and transformed NIH cells for sequences related to the λ ChBlym-1 transforming gene.

M13R9 probe was also hybridized to molecular clones of the retroviral transforming genes *abl*¹², *erb*¹³, *fes*¹⁴, *fms*¹⁵, *mos*¹⁶, *myb*¹⁷, *myc*¹⁸, *ras*¹⁹, *ras*^{K20}, *rel*²¹, *sis*²² and *src*²³. No hybridization was detected (not shown), indicating that the

transforming gene of λ ChBlym-1 is not homologous to the transforming genes of these sarcoma and acute leukaemia viruses.

Nucleotide sequence of the transforming region

The above analysis of pHR indicates that transforming sequences were located in the region spanned by the two *Ava*II sites and that this region of the clone was homologous to a discrete family of conserved cellular DNA sequences. Preliminary results also indicated that these sequences were expressed at low levels in cytoplasmic polyadenylated RNA in RP9 lymphoma cells and in NIH cells transformed by RP9 DNA (manuscript in preparation). Since these results indicated that this region of the clone was responsible for transforming activity, its nucleotide sequence was determined (Fig. 4).

Deletion clones of pHR and pRA were constructed by *Bal*31 digestion, subcloned in M13 vectors²⁴ and sequenced by a modification of the dideoxy chain termination method of Sanger²⁵ (Fig. 4). About 45% of the sequence was determined from both strands. When sequence was determined from one strand only, the analysis was repeated at least twice. The nucleotide sequence of this region (Fig. 4) confirms the presence and absence of all restriction sites previously mapped.

At positions 538 and 567, two poly(A) addition signals (AATAAA)²⁶ were found, suggesting the location of the 3' end of the message near the right *Ava*II site (position 575–579). This location is consistent with the observation that no hybridization with RP9 RNA was detected using a probe extending from the right *Ava*II site to the end of the clone (data not shown).

About 550 nucleotides upstream, two signals associated with eukaryotic promoters are found: an AT rich region of 10 nucleotides at position 91–100 (TATA box) and a sequence CCAAAT at position 15–20^{25–29}. The distance between these sequences (about 70 nucleotides) is similar to that separating homologous sequences in promoters of other eukaryotic genes. If these sequences define the promoter of the transforming gene, transcription would be expected to initiate approximately 25 nucleotides downstream of the TATA box (around position 120–130). The first ATG codon in this transcript is at position 176 and would represent a likely site for initiation of translation. This reading frame is terminated by the codon TAA at position 215. However, the presence of two consensus sequences for 5' (AT/GTTA) (201–206) and 3' (CAG) (241–243) splice sites³⁰ suggests that 41 nucleotides are removed during maturation of the transcript. If this processing event occurred, translation would proceed in the single major open reading frame of the

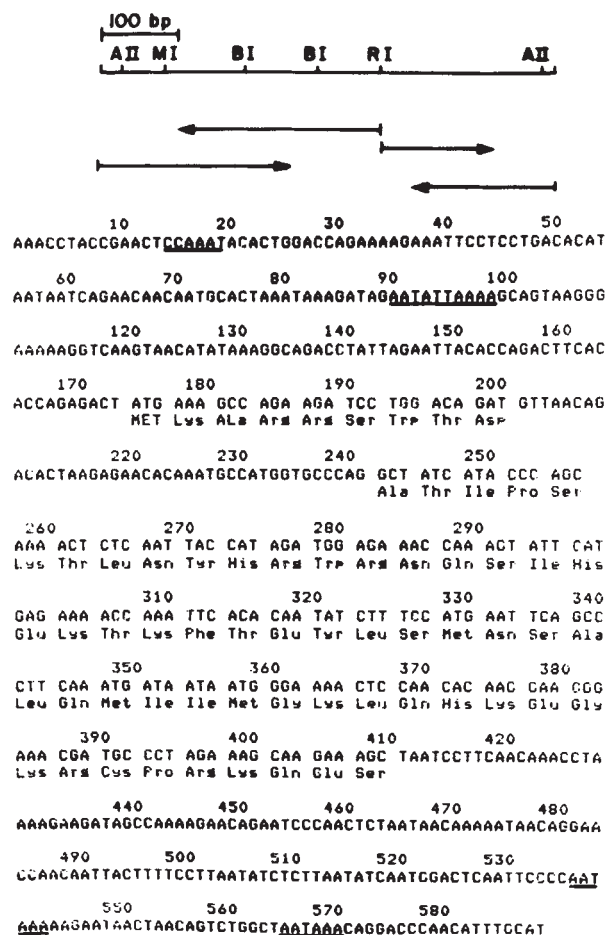


Fig. 4 Nucleotide sequence of the transforming region of λ ChBlym-1. pHR and pRA were cleaved with *Hind*III and digested with *Pseudomonas* Bal31 nuclease for various times⁵⁷. *Hind*III linkers were ligated to the termini and the plasmids were recircularized and used to transform *E. coli* strain HB101. Two deleted clones of pHR and two deleted clones of pRA were isolated. The largest inserts were subcloned in the mp8M13 vector and the shortest in the mp9M13 vector. The inserts of these M13 subclones are the following: M13R9, 252 nucleotides to the right of the *Eco*RI site in mp8; M13R6, 152 nucleotides to the right of the *Eco*RI site in mp9; M13-4B, 197 nucleotides to the left of the *Eco*RI site in mp9; and M13-16, 335 nucleotides to the left of the *Eco*RI site in mp8. The inserts of M13R9 and M13-4B are of the same polarity as the nucleotide sequence shown, whereas the inserts of M13R6 and M13-16 are complementary to the indicated sequence. The direction and extent of sequencing for each DNA fragment is indicated by arrows underneath the restriction map of the sequenced region. Nucleotide sequencing was performed by the method of Sanger²⁵ as modified by S. K. Karathanasis (personal communication) to use reverse transcriptase. Sequences associated with eukaryotic promoters and poly(A) addition sites are underlined. The positions of the restriction sites indicated above are: *Ava*II, 26–30 and 575–579; *Mn*II, 43–46; *Bst*NI, 192–196 and 240–244; *Eco*RI, 332–337. The amino acid sequence of the putative protein product is indicated beneath the nucleotide sequence.

sequence to a termination codon (TAA) at position 412. The predicted translation product of this sequence is a 65 amino acid protein (molecular weight $\sim 7,800$) whose amino acid sequence is indicated in Fig. 4. The predicted protein is rich in lysine (12.3%) and arginine (9.2%). It is hydrophilic at both termini but contains an internal region of 14 hydrophobic amino acids.

Homology of the transforming protein sequence to transferrin

A computer-assisted homology search³¹ was performed to investigate possible relationships between the predicted amino

acid sequence of the λ ChBlym-1 transforming protein and amino acid sequences of known cellular proteins. This analysis revealed significant homology between the λ ChBlym-1 transforming protein sequence and proteins of the transferrin family (Fig. 5).

Transferrins are high molecular weight ($\sim 80,000$) iron-binding proteins. The amino acid sequences of human serum transferrin, human lactoferrin and chicken ovotransferrin indicate that these proteins are homologous to each other and that they have evolved by a gene duplication such that the carboxy- and amino-terminal halves of each of these proteins show a high degree of homology^{32–36}. The partial amino acid sequence of a protein recently identified as a melanoma surface antigen (p97) has indicated that this protein is also a member of the transferrin family³⁷.

Figure 5 displays the homology between the predicted amino acid sequence of the λ ChBlym-1 transforming protein and the amino-terminal regions of these members of the transferrin family. Sequences of both the amino- and carboxy-terminal halves of human transferrin, lactoferrin and ovotransferrin are shown. The amino-terminal sequences of these transferrin proteins represent the sequences of the secreted proteins after removal of the signal peptide.

The amino acid sequence of the λ ChBlym-1 protein beyond the predicted splice site (which occurs between amino acids 9 and 10) is significantly homologous to these members of the transferrin family. Of the 56 amino acids after the splice site of the λ ChBlym-1 protein, 20 are homologous to at least one of the transferrin family proteins. There is no homology between the signal peptide sequence of ovotransferrin and the 5' domain on the amino-terminal side of the splice site of λ ChBlym-1. By the method described by Doolittle³¹, the homology of the λ ChBlym-1 protein to the corresponding region of the N-terminal half of human transferrin was significant at the $P = 0.05$ level. This relationship becomes more striking when relationships between other family members are also considered. For example, the lower part of Fig. 5 displays the extent of homology of the λ ChBlym-1 protein with the amino-terminal halves of ovotransferrin, lactoferrin and p97, and with the carboxy-terminal halves of human transferrin, ovotransferrin and lactoferrin (solid line). This is compared with the extent of homology between the corresponding region in the amino-terminal half of human transferrin and the same six other transferrin family sequences (dashed line). It is apparent from this type of analysis that there is a pattern of sequence conservation and divergence between transferrin and the other related members of the family, and that this same pattern of homology is evident in the putative λ ChBlym-1 protein. Thus, the highest degree of homology to other transferrin family members occurs within the amino-terminal half of the indicated sequence of both the λ ChBlym-1 transforming protein (11/26 amino acids) and human transferrin (16/26 amino acids). In contrast, the next 26 amino acids of both the λ ChBlym-1 protein and human transferrin display a lower degree of scattered homology with the other transferrin family sequences, although the carboxy-terminal portions of both the λ ChBlym-1 protein and human transferrin again appear significantly homologous to other transferrin sequences. Comparison of the nucleotide sequence of the putative coding region of λ ChBlym-1 with that of ovotransferrin mRNA³⁵ shows the same pattern of homology as the amino acid sequence (not shown). These relationships suggest a common ancestry for the transforming protein of λ ChBlym-1 and the amino-terminal sequences of members of the transferrin family, and stimulate speculation concerning possible functional similarities.

Conclusions

We have isolated and characterized a biologically active transforming gene detected by transfection of chicken B cell lymphoma DNA. This transforming gene is homologous to a small family of normal cell genes which are highly conserved in vertebrate evolution. Due to this high degree of sequence

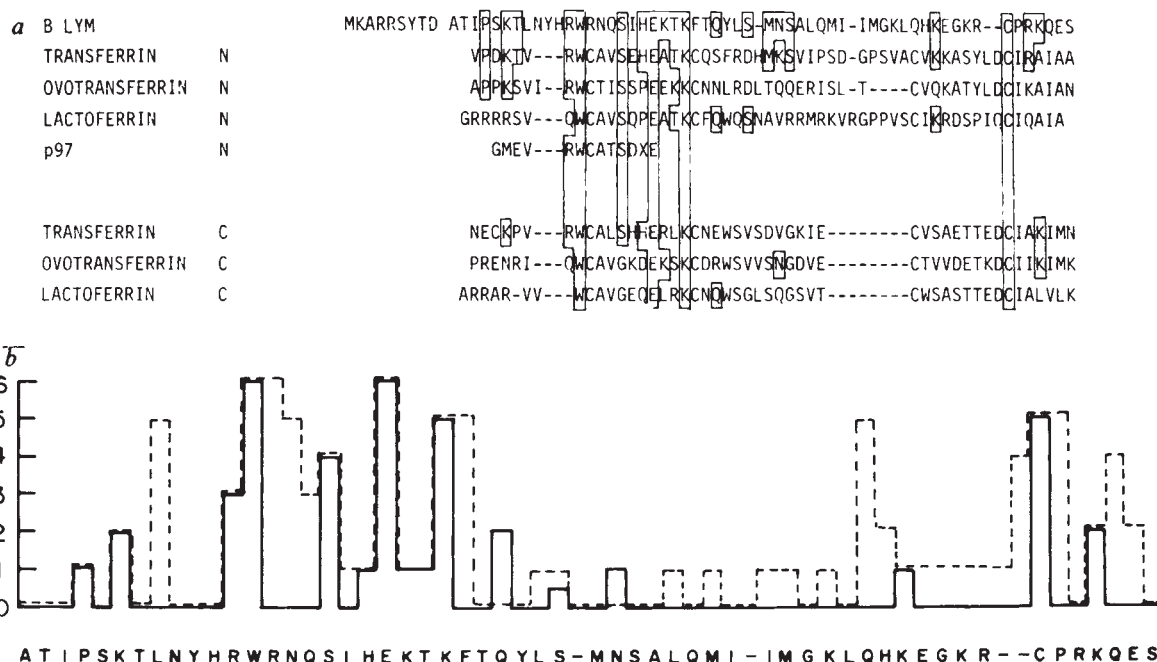


Fig. 5 Homology between the predicted transforming protein of λ ChBlym-1 and proteins of the transferrin family. *a*, The amino acids of the λ ChBlym-1 transforming protein (B lym) which are homologous to other transferrin family proteins are enclosed in boxes. The splice site in the λ ChBlym-1 transforming sequence occurs between aspartate (D) and alanine (A) and is indicated by a blank in the sequence. Only the homologous amino terminal regions of both the amino (N)- and carboxy (C)- terminal halves of human transferrin³², chicken ovotransferrin^{35,36} and human lactoferrin^{33,34} are shown. p97 is a melanoma surface protein which is also related to transferrin³⁶. *b*, The amino acid sequences of the λ ChBlym-1 transforming protein (—) and of the amino-terminal domain of human transferrin (---) are compared separately with the amino acid sequences of ovotransferrin N, lactoferrin N, p97, transferrin C, ovotransferrin C and lactoferrin C. The λ ChBlym-1 amino acid sequence is indicated beneath the graph. The extent of homology at each position is presented on a scale of 0–6 to indicate the number of other transferrin family sequences containing the same amino acid.

conservation, and to the presence of sequences partially homologous to mouse satellite DNA, we were not able to determine the species of origin of the λ ChBlym-1 transforming gene by blot hybridization analysis. Although we cannot, therefore, exclude the possibility that this transforming gene is derived from transformed NIH cells, rather than from the primary chicken lymphoma, we consider this unlikely for several reasons. First, serial transmission of transforming genes in primary and secondary transfection assays has established in several systems that the same transforming gene is detected by transfection of DNAs of both primary neoplasms and transformed NIH cells¹. Second, the transcription of λ ChBlym-1 sequences in both chicken lymphoma cells and NIH cells transformed by chicken lymphoma DNA is consistent with a chicken lymphoma origin of the gene. Third, a chicken lymphoma origin is further supported by detection of the putative λ ChBlym-1 transforming protein in both lymphoma cells and NIH cells transformed by lymphoma DNA (see below).

The high degree of evolutionary conservation observed for the transforming gene of λ ChBlym-1 is also characteristic of cellular homologues of retrovirus transforming genes. However, with the exception of the *ras* gene family, the cellular homologues of retroviral transforming genes are present as single copies in normal cell DNAs^{19,38}. In addition, no homology was detected between the transforming gene of λ ChBlym-1 and the transforming genes of 12 distinct retroviruses, including *ras*^H and *ras*^K. The transforming gene of λ ChBlym-1 thus seems to represent a new transforming gene which is unrelated to viral transforming genes or to the transforming genes detected by transfection of human bladder and lung carcinoma DNAs, which are cellular homologues of viral *ras* genes^{39–41}. Since the cellular gene family homologous to the λ ChBlym-1 transforming gene is conserved in human DNA, it will be of interest to investigate the possible relationships between the members of this gene family and the different transforming genes detected by transfection of DNAs of human and mouse neoplasms representative of discrete states of B- and T-lymphocyte differentiation⁴².

The nucleotide sequence of the λ ChBlym-1 transforming gene indicates that it encodes a small protein (molecular weight 7,800) which is homologous to the amino-terminal region of proteins of the transferrin family. Transferrin, an iron-binding protein of molecular weight approximately 80,000 daltons, is present in serum of all vertebrates and is an essential growth factor for cells in serum-free medium. Expression of a transferrin-related surface antigen³⁷ and of transferrin receptors^{43–49} is closely correlated with proliferation of both normal and neoplastic cells, suggesting a possible involvement of these receptors in control of cell proliferation. In addition, transferrin has been reported to stimulate growth of lymphocytes independently of its iron transport activity^{50–52}. If the homology of the small protein encoded by the λ ChBlym-1 transforming gene to transferrin reflects a functional relationship, it is thus attractive to speculate that the λ ChBlym-1 protein may function via interaction with a cellular regulatory system related to transferrin.

Preliminary experiments indicate that an affinity purified antiserum prepared against a synthetic carboxy-terminal decapeptide of the predicted λ ChBlym-1 amino acid sequence recognizes a protein in extracts of RP9 cells and NIH cells transformed by RP9 DNA, but not in NIH 3T3 cells, spontaneously-transformed NIH cells or normal bursal lymphocytes (S. Welch, R. Eisenman, P. E. Neiman, G. Goubin and G. M. Cooper, manuscript in preparation). The molecular weight of this protein in RP9 cells is approximately 8,000. These findings are consistent with the predictions of the nucleotide sequence and should permit further studies of the lymphoma transforming protein.

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Retrovirus-like particles containing RNA homologous to the transposable element *copia* in *Drosophila melanogaster*

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The presence in cultured Drosophila melanogaster cells of retrovirus-like particles containing 5 kilobase RNA molecules homologous to the transposable element copia provides support for the suggested evolutionary relationship between retroviruses and eukaryotic movable genetic elements.

MOVABLE, or transposable, genetic elements have been identified in a number of prokaryotic and eukaryotic organisms¹⁻⁵. Transposable elements with similar properties to the one termed *copia* have been shown to account for several per cent of the total genome of *Drosophila melanogaster*. Recent observations have revealed that these *copia*-like elements share some important structural features with the integrated, proviral form of vertebrate retroviruses⁶⁻¹⁷, leading to the suggestion of an evolutionary relationship between retroviruses and transposable elements.

So far, however, no infectious retroviruses have been found in *Drosophila*, although the possible presence of retrovirus-like particles has been pointed out. Enzymatic activity similar to that of reverse transcriptase, an enzyme characteristic of vertebrate retroviruses, has been found partly associated with particles from *D. melanogaster* cultured cells reminiscent of vertebrate retroviral A-type particles¹⁸. We have isolated and purified the so-called virus-like particles (VLPs)^{19,20} that have been identified by electron microscopy in *D. melanogaster* cells^{21,22}. Isolated VLPs are spherical in shape, with a diameter of approximately 50 nm, and consist of protein and RNA, with 4S, 4.5S, 5S and 6S molecules as the major RNA constituents.

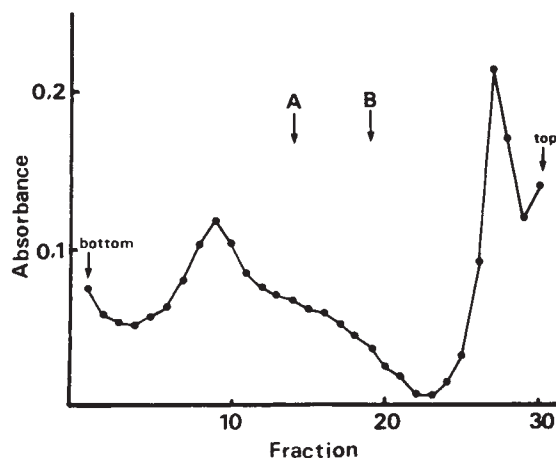
It was speculated that the VLPs might represent a defective form of a *Drosophila* RNA virus whose genome is integrated as DNA into a host chromosome. Here we describe results demonstrating that VLPs contain high molecular weight RNA molecules homologous to the *copia* element, and which can be translated *in vitro* into polypeptides immunologically related to the VLPs themselves. We also present evidence that VLPs have an associated reverse transcriptase-like activity. Thus, although the infectivity (or lack of it) of VLPs remains to be demonstrated these appear to have at least some of the characteristics required for their classification as a *Drosophila copia*-related retrovirus.

The detection and analysis of *copia*-related RNA from VLPs

The method of VLP purification from the nuclei of cultured *D. melanogaster* (GM₂) cells was essentially as described previously¹⁹, and is described in Fig. 1 legend. The presence of various species of low molecular weight RNAs in VLPs has already been mentioned^{19,20}. In this work, high molecular weight RNAs, with a size range from 15S to 35S, were found for the first time associated with VLPs (Fig. 1). Hereafter, this

Fig. 1 A typical sedimentation pattern of VLP RNA. The arrows labelled A and B indicate the positions of 23S and 16S *Escherichia coli* ribosomal RNAs respectively, and were determined by a parallel run.

Methods: VLP was purified essentially in the manner described previously¹⁹. GM₂ cells were cultured in suspension using 5 l of D20 medium containing 13% precolostrum calf serum¹⁹. Cells were collected by low-speed centrifugation on day 4 or 5 of the stationary phase (cell density 3×10^6 cells ml⁻¹). Nuclei were then isolated according to the procedures described by Wray and Stubblefield³⁸ and sonicated 10 times on ice for 30 s each at 50 W. In our experimental conditions, more than 90% of the nuclei were found to be disrupted. After the debris was removed by low-speed centrifugation (10,000g, 20 min, 4°C), VLP was precipitated by a high-speed centrifugation (70,000g, 2 h, 4°C). For mild suspension of VLP, the pellet was maintained overnight at 4°C in a small amount of TMN buffer (10 mM Tris-HCl pH 7.2, 5 mM MgCl₂ and 0.1 M NaCl). The VLP suspension was then centrifuged at 10,000g for 10 min to remove debris, and the supernatant was subjected to centrifugation in 5–20% (W/V) sucrose gradient in TMN buffer at 2.5×10^4 r.p.m. for 75 min at 4°C. Fractions were collected from the bottom of the tube and analysed for absorbance at 260 nm, yielding a single peak around 150S (see Fig. 5). The peak fractions (usually three to five fractions) were collected, diluted fivefold by TMN buffer, and recentrifuged at 4×10^4 r.p.m. for 1.5 h. The VLP pellet was resuspended in TMN buffer and subjected to another cycle of a sucrose gradient centrifugation. Although in some initial experiments VLP was banded in a metrizamide gradient (density of VLP in metrizamide 1.27 g ml⁻¹), it was later noticed that this step could be omitted. Agarose gel electrophoresis (see Fig. 2a legend) verified the absence of appreciable contamination by free RNA of the VLP preparations thus obtained. Calculated in terms of RNA, a typical yield of VLP was about 250 µg per 5 l culture. The VLP RNA was extracted by the hot phenol method³⁹. After the purified VLP was treated with 0.2% SDS at 30°C for 15 min, the VLP RNA was extracted twice by shaking with an equal volume of water-saturated distilled phenol (at 60°C for 10 min) and then precipitated by adding ethanol to the aqueous phase. Approximately 100 µg of VLP RNA was then layered on a 10–30% (W/V) sucrose gradient containing 10 mM Tris-HCl (pH 7.2) and 5 mM MgCl₂, and centrifuged at 2.5×10^4 r.p.m. for 15 h at 4°C. Fractions were collected from the bottom of the tube and absorbance at 260 nm was measured.



high molecular weight VLP RNA will be referred to as VLP H-RNA.

Figure 2a, lanes 1–3, shows the absence of detectable DNA in nucleic acids extracted from VLPs. VLP RNA is unlikely to consist of cellular RNA bound artificially to VLP for the following reasons: (1) the RNA associated with VLPs was resistant to RNase A, as shown in Fig. 2a, lanes 4–5; (2) no RNA dissociated from VLP could be detected after treatment with 1 M NaCl¹⁹; and (3) only a few per cent of ³²P-labelled cellular RNA added exogenously migrated with VLPs in an agarose gel when the mixture was subjected to electrophoresis¹⁹. It should also be pointed out that the amount of free RNA in the supernatant of the sonicated nuclei of the late stationary state cells from which VLPs are purified was much less than that of the RNA associated with the VLPs (Fig. 2a, lane 13).

The total RNA extracted from the VLPs was analysed by agarose gel electrophoresis in the presence of 5 M urea (Fig. 2b, lane 1). In the VLP H-RNA fraction, a distinct band of approximate size 5 kilobases (kb) was found, together with a relatively high background (smear), suggesting that VLP H-RNA consists of one major RNA species having a length of 5 kb, and either its breakdown products or a heterogeneous population of other minor RNA species of various molecular lengths, or both. Chromatography on oligo(T) cellulose suggests that only a portion of VLP H-RNA is polyadenylated (data not shown).

To determine whether VLP H-RNA is cellular in origin, as in the case of its low molecular weight counterparts (unpublished data), *D. melanogaster* genomic DNA was isolated and subjected to blot hybridization²³ using VLP H-RNA as a probe. In Fig. 2c, lanes 1–3, many bands can be recognized, suggesting that nucleotide sequences homologous to VLP H-RNA are present at various sites on the chromosome. In a similar experiment using *D. virilis* and calf thymus DNAs (Fig. 2c, lanes 4, 5) no visible bands were detected, which is consistent with the previous result¹⁹ that *D. virilis* has no detectable VLPs.

Forty-seven recombinant clones whose DNA inserts were hybridizable with VLP H-RNA were isolated from 2×10^4 phages in a cloned *D. melanogaster* genome library^{24,25}. The restriction maps of 17 of these clones were constructed, and some typical examples are shown in Fig. 3a. The structures of the regions homologous to VLP H-RNA are quite similar to

each other, but not those of the flanking regions. Since the DNA segments containing movable genetic elements have similar properties, inspection of the available restriction maps of various *D. melanogaster* movable genetic elements was carried out as the first step in a search for VLP H-RNA genes. As can be seen in Fig. 3b, the maps of the *copia* elements in cDm 2055²⁵, cDm 2056 and cDm 2087²⁶ are the same as those for DNA homologous to VLP H-RNA in most of the clones shown in Fig. 3a, suggesting that the gene that encodes VLP H-RNA might be movable genetic element *copia*.

DNA extracted from nine of the recombinant clones was digested with restriction enzymes *EcoRI* and *HpaI*, sized by electrophoresis on an agarose gel and analysed by Southern blot hybridization²³. It can be seen in Fig. 3c that the blotting profiles obtained using VLP H-RNA as a hybridization probe (left panel) are quite similar to those obtained with the cDm 2055²⁵ probe (right panel), containing an authentic *copia* sequence. In a separate experiment, all other recombinant clones were found to have DNA fragments hybridizable with the *copia* sequence. The total RNA extracted from the VLPs was assayed for *copia* sequences by agarose gel electrophoresis followed by Northern hybridization²⁷. Figure 2d, lanes 1, 2, clearly shows that RNA homologous to *copia* elements is included in the VLP H-RNA fraction. A similar experiment using cDm 4010²⁵ containing another *Drosophila* movable genetic element, 297, was also carried out. However, in this case, no positive signal was detected (Fig. 2d, lane 3). Preliminary experiments also suggest that the VLPs contain no detectable RNA homologous to the *Drosophila* movable genetic elements 412¹⁵ and 17.6⁴⁵. These results, along with the finding described below that *copia* DNA can almost completely arrest *in vitro* translation directed by VLP H-RNA, strongly suggest that most, if not all, of the high molecular weight RNA encapsidated in VLPs consists of 5 kb long transcripts of *copia* elements and their derivatives.

VLP *copia*-related RNA can direct the synthesis of polypeptides precipitable with anti-VLP serum

VLPs contain at least several species of protein molecules, including a predominant 31,000 molecular weight (31K) protein

Fig. 2 a, Susceptibility of VLPs, and of the nucleic acids extracted from them, to DNase and RNase digestion. The figure shows a UV photograph of an ethidium bromide stained agarose gel in which the following had been electrophoresed: lane 1, VLP RNA (1 μ g) without treatment; lane 2, VLP RNA treated with RNase; lane 3, VLP RNA treated with DNase; lane 4, VLP (0.5 μ g as RNA) without treatment; lane 5, VLP treated with RNase; lane 6, VLP treated with DNase; lane 7, *E. coli* phage, MS2 RNA (2 μ g) without treatment; lane 8, MS2 RNA treated with RNase; lane 9, MS2 RNA treated with DNase; lane 10, MS2 particles (3 μ g as RNA) without treatment; lane 11, MS2 particles treated with RNase; lane 12, MS2 particles treated with DNase; lane 13, crude preparation of VLP (a portion of the supernatant of the nuclear sonicate, corresponding to 10 ml culture, was applied without further treatment). Arrows labelled A, B and C indicate the positions of VLP, the MS2 phage and free RNA, respectively. **b**, Agarose gel electrophoresis of VLP RNA. Lane 1, total VLP RNA (5 μ g); lane 2, *E. coli* 23S (3 kb) and 16S (1.5 kb) RNAs with low molecular weight RNAs; lane 3, MS2 RNA (3.6 kb); lane 4, tobacco mosaic virus RNA (6 kb). Arrows labelled A and B indicate the positions of the 5 kb VLP H-RNA and low molecular weight VLP RNA, respectively. **c**, Blot hybridization patterns using labelled VLP H-RNA as a probe. Lane 1, GM₂ cell DNA digested with *Eco*RI; lane 2, GM₂ cell DNA digested with *Bam*HI; lane 3, GM₂ cell DNA digested with *Hind*III; lane 4, *D. virilis* DNA digested with *Eco*RI; lane 5, calf thymus DNA digested with *Eco*RI. Molecular sites in kb are shown on the left. **d**, Northern blot hybridization with VLP H-RNA, using as probes ³²P-labelled cDm2055 (*cop*ia) DNA (lane 2), or cDm4010 (297) DNA (lane 3). Lane 1 shows a UV light photograph of the ethidium bromide stained gel used in the Northern blot. Arrows labelled A, B, C, D and E show, respectively, 4S RNA, 4.5S RNA, 5S RNA, 6S RNA and VLP H-RNA.

Methods: **a**, RNA and virions were electrophoresed in Tris-phosphate buffer¹⁹ on 0.8% agarose gels at 2–3 V cm⁻¹ for 4 h. After electrophoresis, the gels were stained with 0.5 μ g ml⁻¹ ethidium bromide for 30 min, and photographs were taken under UV light. Treatment with RNase A (1 μ g ml⁻¹) or DNase (1 μ g ml⁻¹) was carried out at 37 °C for 30 min. MS2 particles and RNA were used for enzyme control and mobility markers. **b**, The various RNAs were electrophoresed in a 1% agarose gel in Peacock buffer containing 5 M urea³¹ at 35 mA for 3.5 h and at 4 °C. The gels were stained with 0.5 μ g ml⁻¹ of ethidium bromide for 30 min and then photographed under UV light. **c**, The digested DNA was subjected to 0.8% agarose gel electrophoresis and then transferred to a nitrocellulose filter and blot hybridized²³ using as a probe VLP H-RNA labelled *in vitro* by alkali-cleavage and treatment with polynucleotide kinase and [γ -³²P]ATP⁴⁰. Hybridization was carried out in 4 $\times$ SSC, 10 mM potassium phosphate buffer (pH 7.0) containing 50 μ g ml⁻¹ of *E. coli* phage Q β RNA at 65 °C for 36 h. **d**, The total VLP RNA was sized on 10% polyacrylamide gel by electrophoresis⁴¹, stained with ethidium bromide, transferred to diazotized paper²⁷ and then blot hybridized with the appropriate probe. Hybridization was carried out in 50% formamide containing 5 $\times$ SSC, 25 mM sodium phosphate buffer (pH 6.5), 0.2% sodium lauryl sulphate, 50 μ g ml⁻¹ of sonicated salmon sperm DNA, 1% glycine, 0.02% polyvinyl pyrrolidone, 0.02% bovine serum albumin and 0.02% Ficoll. The filter papers were washed at least four times with 5 $\times$ SSC and 50% formamide for 1 h each at 42 °C.

(Fig. 4, lane 1). As one major, and some minor, proteins can interact specifically with anti-VLP antibodies (compare lanes 2 and 3), not only one major but also some minor VLP proteins may be located on the surface of VLPs.

To test whether VLP H-RNA can be translated into polypeptides related to those contained in VLPs, isolated VLP H-RNA was added to a mRNA-dependent rabbit reticulocyte lysate²⁸. The translation efficiencies of VLP H-RNA for polypeptides with molecular weights >10,000 appears to be approximately 1/90th that of tobacco mosaic virus (TMV) RNA (see Fig. 4, lane 8). The translation products were analysed by electrophoresis in 12.5% polyacrylamide gels in the presence of sodium lauryl sulphate²⁹. Seven major polypeptides were reproducibly detected (Fig. 4, lanes 5, 10). Of these, six seem to be specific to VLP H-RNA, no corresponding component being detected in the absence of exogenous RNA (Fig. 4, lane 4). The electrophoretic mobilities of some of the major polypeptides synthesized *in vitro* coincided with those of the VLP proteins, including the major 31K protein.

The precipitability of the *in vitro* translation products by anti-VLP serum was also examined (Fig. 4, lane 6). Several bands, including the one thought to correspond to the major VLP protein, were precipitated by anti-VLP serum. No polypeptide synthesized *in vitro* could be precipitated by preimmune serum (lane 7), and none of the polypeptides synthesized *in vitro* by TMV RNA could be precipitated by anti-VLP serum (lanes 8, 9). (The precipitation of a tiny fraction of the most

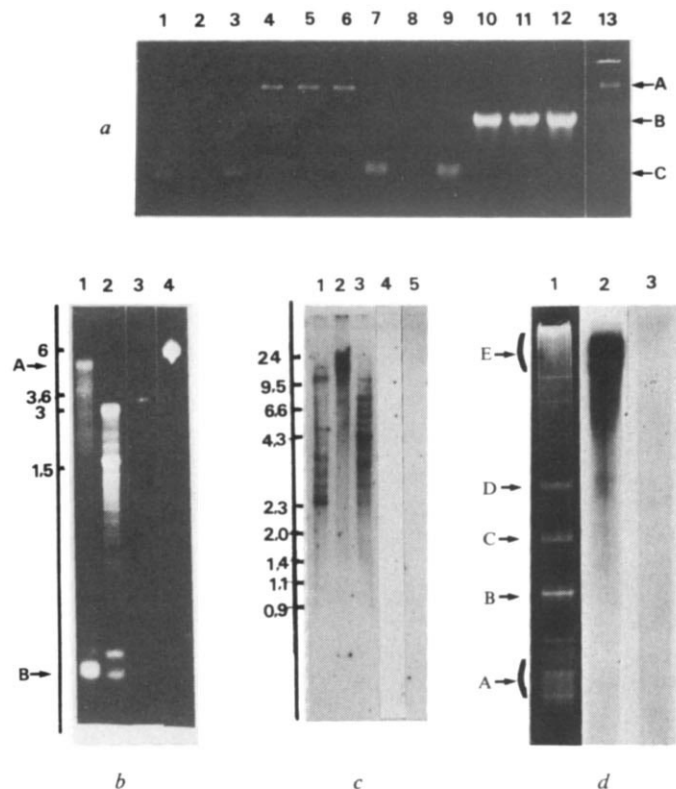


Table 1 Assays for reverse transcriptase-like activity associated with VLPs

Template	³ H-substrate	³ H-triphosphate incorporated (c.p.m.)
* Poly(rA) · oligo(dT) ₁₂₋₁₈	dTTP	15,400
* Poly(rC) · oligo(dG) ₁₂₋₁₈	dGTP	3,615
* Poly(rCm) · oligo(dG) ₁₂₋₁₈	dGTP	1,420
* None added	dGTP	153
		³² P-dGTP incorporated (c.p.m.)
† VLP (–RNase treatment)		31,393
† VLP (+RNase treatment)		10,289
† Without VLP		2,149

* Assays to determine the template/primer preference of the VLP reverse transcriptase-like activity. The reaction conditions are essentially as described in Fig. 5 legend. The concentration of template/primer added was 1 μ g ml⁻¹, and the total amount of VLPs used per assay was the equivalent of 5 μ g as RNA. Incubation was for 1 h at 25 °C.

† Assays to determine the endogenous reverse transcriptase-like activity of VLPs. The assay conditions were essentially as described by Heine *et al.*¹⁸, with incubation for 3 h at 25 °C. For RNase treatment the VLPs were preincubated with a mixture of 1 mg ml⁻¹ RNase A and 1,000 units ml⁻¹ RNase T₁ at 37 °C for 30 min.

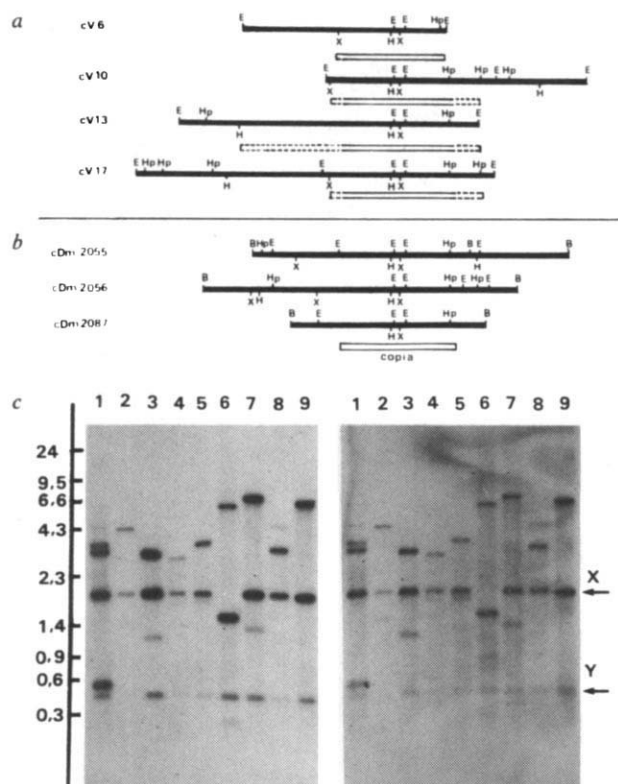


Fig. 3 **a**, Restriction maps of some of the cloned DNA segments hybridizable with labelled VLP H-RNA. The ^{32}P -labelled VLP H-RNA probe was prepared by alkali-cleavage and treatment with polynucleotide kinase and $[\gamma\text{-}^{32}\text{P}]\text{ATP}$ ⁴⁰. The regions homologous to VLP H-RNA, shown by open rectangles below each map, were determined by the blot hybridization results, assuming no intervening sequences in a given region. **b**, Restriction maps of the *copia* elements in cDm 2055²⁵, cDm 2056 and cDm 2087²⁶. Locations of *copia* elements are indicated by open rectangle. E, *EcoRI*; H, *HindIII*; X, *XbaI*; B, *BamHI*; Hp, *HpaI*. **c**, Blot hybridization of nine of the VLP H-RNA positive clones (cV1 to cV9 in lanes 1 to 9) with probes specific for VLP H-RNA (left panel) and *copia* (right panel) sequences. Molecular sizes are shown on the left in kb. The arrows labelled X and Y on the right show, respectively, the positions of the 1.85 kb and 0.45 kb *EcoRI/HpaI* fragments common to most *copia* elements.

Methods: Recombinant clones having DNA inserts hybridizable with VLP H-RNA were isolated from a cloned *D. melanogaster* genome library described previously²⁵. DNA extracted from nine recombinant clones was digested with *EcoRI* and *HpaI*, sized on 0.8% agarose gels by electrophoresis, transferred to a nitrocellulose filter and blot hybridized using as probes ^{32}P -labelled VLP H-RNA or cDm 2055 (*copia*) DNA prepared as described previously²⁵ from *E. coli* HB 101 (cDm 2055). The conditions for hybridization are described in the legend to Fig. 2c and elsewhere²⁵ for RNA and DNA probes, respectively.

major TMV protein synthesized *in vitro*, whose location is labelled by an asterisk in lane 9, was interpreted as the result of a nonspecific interaction with the serum). Thus VLP H-RNA seems capable of acting as an mRNA for the synthesis of at least some of the VLP proteins.

In a previous section, it was shown that *copia*-related RNA accounted for the majority of the VLP H-RNA. The fact that *copia* DNA can be demonstrated to arrest almost completely the *in vitro* translation of VLP H-RNA, indicates that it is the *copia*-related sequence present in VLP H-RNA that is actually translated into VLP-related polypeptides. VLP H-RNA was annealed with heat-denatured DNA segments containing *copia* or non-*copia* sequences and then added to an *in vitro* translation system. As can be seen in Fig. 4, lanes 10 and 11, all bands corresponding to the translation products of VLP H-RNA are markedly reduced, or have disappeared, on treatment with *copia* DNA, whereas no appreciable change in banding patterns

(except for a 29,000 molecular weight protein) was observed on treatment with pBR322 DNA (lane 13). As most of the bands reappeared following dissociation of the RNA-*copia* DNA hybrids (lane 12), it is obvious that nearly all the polypeptides synthesized *in vitro* and precipitable with anti-VLP serum must be translated from the VLP H-RNA sequence homologous to *copia*.

In vitro translation of *copia* RNA has also been reported using *copia* RNA extracted from the cytoplasm of *Drosophila* cultured cells^{28,30}. The gel electrophoretic patterns of *in vitro* translation products obtained are similar, but not always identical, to those reported here using VLP *copia* RNA. It has also been reported that cytoplasmic *copia* RNA is a weak mRNA and that only 2 kb *copia* RNA can act as an active mRNA²⁸. In contrast, no 2 kb RNA was detected as a distinctive component in our VLP H-RNA preparations. These differences might arise in part from the sequence heterogeneity of both *copia* RNA³¹ and DNA^{6,32}. It is also possible that the differences resulted from the fact that our VLP *copia*-related RNA belongs to a particular population of nuclear *copia* RNA that represents the majority of the total cellular *copia* RNA, whereas the cytoplasmic *copia* RNA examined by other investigators represents less than 20% of the total *copia* RNA³².

The association of reverse transcriptase-like activity with VLPs

The endogenous retroviral particles of vertebrates are generally associated with reverse transcriptase activity^{33,34}. We have examined whether our *Drosophila* VLPs have a similar activity. Purified VLPs were subjected to sucrose gradient centrifugation, and the presence of reverse transcriptase (or similar) activity across the gradient was assayed for using poly(rA)-oligo(dT) as the template and primer (Fig. 5). The concentration of VLPs in each fraction was also determined, by both absorbance at 260 nm and the agarose gel assay described in Fig. 2a legend. Except for some top fractions, the profile of the distribution of the enzyme activity was generally identical to that of the VLP content. The enzyme associated with the VLPs could also effectively use as template/primers poly(rC)-oligo(dG), a poor substrate for DNA polymerase γ (ref. 35), and poly(2'-O-methylcytidylate)-oligo(dG), which has been reported³⁶ not to be used by DNA polymerase γ (Table 1). Thus, *Drosophila* VLPs seem to contain reverse transcriptase-like activity, although the properties of the RNase sensitive, endogenous substrate remain to be clarified (Table 1). Our preliminary data also suggest that the enzyme requires a divalent ion, and that the optimum temperature, as for *Drosophila* cell growth, is around 25 °C.

VLPs are viral particles related to *copia* retrovirus

Like the integrated proviral forms of vertebrate retroviruses the movable genetic element *copia* consists of an internal segment (4.5 kb long) flanked by long terminal direct repeats, has the terminal dinucleotides 5' TG...CA 3', and is flanked by short, direct repeats of host DNA⁶. If *Drosophila* contains retroviral particles whose provirus is *copia*, then by analogy with retroviruses in vertebrates, they should have the following properties. (1) They should contain full-length (5 kb) *copia* RNA. (2) Either the *copia* RNA encapsidated in the particles or its cut and spliced product(s) should direct the synthesis of polypeptides consisting of viral particles. (3) The particles should contain reverse transcriptase activity. (4) The particles should be infectious to *Drosophila* cells. Our data in the previous sections show that VLPs have properties (1), (2) and (3). Whether or not VLPs are infectious remains unclear, although a preliminary experiment suggests that VLPs have no effect on the growth of GM₂ cells up to an input ratio of 100 VLPs per cell. Furthermore, Flavell and Ish-Horowicz⁸ have recently succeeded in isolating circular copies of *copia* having structures

Fig. 4 Analysis of VLP proteins and VLP H-RNA translation products by polyacrylamide gel electrophoreses. Lane 1, Coomassie blue stained total VLP polypeptides, from an amount of VLPs that would contain approximately 5 μ g RNA. Lanes 2 and 3 show nitrocellulose filters carrying VLPs, transferred from an acrylamide gel, assayed with anti-VLP serum (lane 2), and pre-immune serum (lane 3). Lanes 4–13 show the results of *in vitro* translation experiments. Lanes 4, 5 and 10 show the products of translation using a rabbit reticulocyte system with (lanes 5, 10), and without (lane 4) added VLP H-RNA as the exogenous mRNA. Lanes 6 and 7 show the *in vitro* translation products immunoprecipitated with anti-VLP serum (lane 6) and preimmune serum (lane 7). Lane 8 shows the translation products, and lane 9 the anti-VLP serum precipitated translation products, of a 1:1 mixture of VLP H-RNA and TMV RNA (1 μ g each). Lanes 11 and 13 show the translation products with VLP H-RNA following translation arrest with *copia* DNA (lane 11), and pBR322 DNA addition as a control (lane 13). Lane 12 shows the translation products following dissociation of *copia* DNA from VLP H-RNA. The filled circle marks a 29,000 molecular weight protein the intensity of which is reduced in translation reactions with added pBR322 DNA (reason unknown). Molecular weights ($\times 10^{-3}$) are shown on the left.

Methods: VLPs were purified as described in Fig. 1 legend. After an equal volume of the lysis buffer, consisting of 62.5 mM Tris-HCl (pH 6.8), 2% sodium lauryl sulphate, 5% mercaptoethanol and 0.001% bromophenol blue, was added, the protein was denatured at 100 °C for 2 min and subjected to 12.5% polyacrylamide gel electrophoresis²⁹. For the experiments in lanes 2 and 3 VLP proteins were transferred from the acrylamide gel to nitrocellulose filters, and detected by anti-VLP serum essentially according to the method of Bowen *et al.*⁴². The anti-VLP serum used here was prepared by injecting 1 ml of VLP solution (25 μ g ml⁻¹ as RNA) intravenously eight times at 3–4-day intervals into rabbits. For the *in vitro* translation experiments exogenous RNA was added (if required) to a rabbit reticulocyte lysate (Amersham); polypeptides synthesized *in vitro* and labelled with ³⁵S-methionine were detected by fluorography⁴³. The immunoprecipitations used in the experiments illustrated in lanes 6, 7 and 9 were carried out according to Simmons and Martin⁴⁴. For the translation-arrest experiments (lanes 11–13) the VLP H-RNA was pretreated with denatured DNA (5 μ g) before addition to the translation system, as described by Flavell *et al.*²⁸.

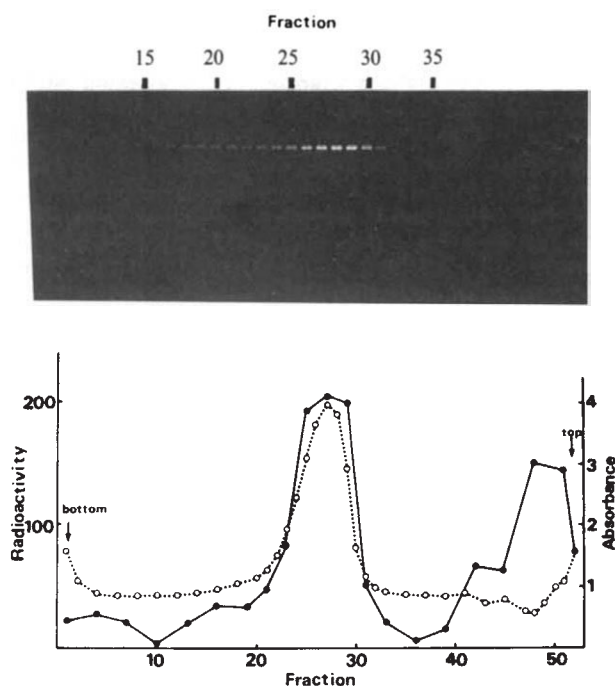
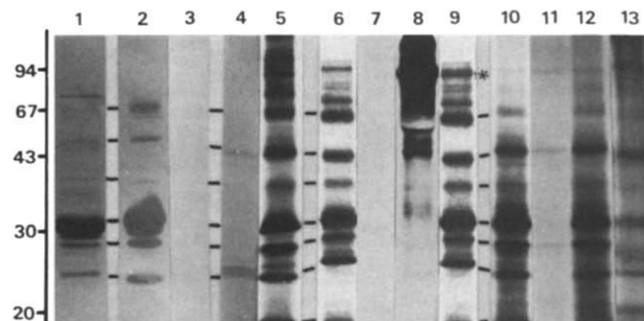


Fig. 5 Sedimentation profiles of VLPs and assay for reverse transcriptase-like activity. ●—●, Reverse transcriptase-like activity (c.p.m.); ○—○, absorbance at 260 nm. The photographs above in the graph shows the results of the agarose gel assay of VLP (see legend to Fig. 2a).

Methods: Purified VLPs (100 μ g as RNA; 670 μ g as protein) were subjected to centrifugation in a 5–20% (w/v) sucrose gradient in 10 mM Tris-HCl (pH 7.2), 5 mM MgCl₂ and 0.1 M NaCl for 75 min at 25,000 r.p.m. and at 4 °C. The fractions were collected from the bottom of the tube, and the reverse transcriptase-like activity and concentration of VLP were measured for each fraction. The reverse transcriptase-like activity was essentially determined according to the method of Heine *et al.*¹⁸, with incubation being carried out at 25 °C for 1 h. The VLP content was measured both by absorbance at 260 nm and by the agarose gel method described in detail in Fig. 2a legend¹⁹.

quite similar to their counterparts in retroviruses. It is very unlikely that these similarities are coincidental.

We thus conclude that VLPs and the transposable *copia* elements are, respectively, direct derivatives of viral particle and proviral forms of '*copia* retrovirus', a putative *Drosophila* retrovirus.

The origin of *copia*-like movable genetic elements in eukaryotes

So far, the partial nucleotide sequences of at least eight *copia*-like movable genetic elements have been determined in *Drosophila* and *Saccharomyces* (refs 6, 11–17, 45). These nucleotide sequences suggest not only that the overall sequence organization of the *copia*-like elements resembles that of vertebrate retroviral proviruses, but also that the degree of sequence similarity varies from element to element. Using important and conserved virus sequences as references we determined the following order of similarity of *copia*-like elements to proviruses: *copia*, *mdg* 3, *Tyl* < *mdg* 1, 412, 17.6, 297, B104 < retroviral proviruses (ref. 45 and unpublished data). That is, *copia* appears to belong to the category of *copia*-like elements least related to vertebrate retroviruses. We have also recently found that the terminal repeat sequence of a *Drosophila* movable genetic element, 17.6, is highly homologous to that of the avian leukosis-sarcoma virus⁴⁵.

It thus seems natural to conclude that *copia*-like movable genetic elements are generally derived from retroviral proviruses long since entrapped in the host chromosomes, and which have lost their original properties to various degrees during evolution. However, our data do not necessarily exclude the possibility that *copia*-like elements are themselves the precursors of RNA tumour viruses³⁷.

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LETTERS TO NATURE

Initial spin and magnetic field of the fast pulsar 4C21.53

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The newly discovered pulsar 4C21.53 is the fastest pulsar known with a period¹ $P \approx 1.6$ ms and a rate of change of period² $\dot{P} \approx 1.3 \times 10^{-19}$. If the spin down rate is due to magnetic dipole radiation from a rotating neutron star its magnetic field is $B \approx 5 \times 10^8$ G. This value is substantially lower than that of all other radio pulsars whose fields lie in the range $\sim 10^{10}$ – 10^{13} G with the majority having fields $\geq 10^{11}$ G. It has been suggested³ that 4C21.53 belongs to a class of low-magnetic-field ($\ll 10^{11}$ G) pulsars⁴ which are spun up by accretion in a binary^{3,5}. After accretion ceases such stars could become isolated radio pulsars, as in the case of 4C21.53, or binary radio pulsars depending on whether the binary has disrupted or not. Here we make the alternative and, we believe, simpler suggestion that the neutron star formed in isolation and that it essentially has its original spin and magnetic field.

A remarkable feature of pulsars is that despite their compact sizes (radii $R \sim 10^6$ cm) their angular momenta are much less than that of their progenitors on the main sequence. Furthermore, they are slow rotators in the sense that $\omega^2 R^3 / GM \ll 1$, where ω is the angular velocity and $M \approx 1M_\odot$ its mass. Note that even for the fast pulsar $\omega^2 R^3 / GM$ is ~ 0.1 . It has therefore been suggested⁶ that during late stages of stellar evolution, magnetic field lines would transport angular momentum from the contracting red-giant core to the envelope so that both white dwarfs and neutron stars should be slow rotators. This raises the question as to whether the fast pulsar could have

been formed with such a short period (~ 1 ms). However, the following arguments based on observations suggest that there should have been no difficulty in forming it.

We first note that the Crab pulsar has a period ≈ 0.03 s, only a factor ~ 20 larger than that of the fast pulsar. However, the magnetic field of the latter is a factor $\sim 10^4$ less than that of the former. Thus the progenitor red-giant core of the fast pulsar would have had a correspondingly weaker field, assuming flux conservation, and hence would have been slowed down much less than the corresponding progenitor for the Crab pulsar. We also note that the magnetic white dwarf PG1015+01 has a rotation period of 1.6 h and a magnetic field $\geq 10^6$ G (ref. 7). Thus its angular momentum corresponds to that of a neutron star with a spin period ~ 5 ms and a magnetic field $\geq 10^{12}$ G, assuming it has the same surface magnetic flux ($\sim BR^2$). Both these examples suggest that rapidly rotating ($P \sim 1$ ms) neutron stars can be formed if they have weak magnetic fields ($\ll 10^{12}$ G).

We next ask whether a weakly magnetized neutron star would spin down to periods $\gg 1$ ms after it was formed with a period ≤ 1 ms. We consider three mechanisms for spin down; gravitational radiation, magnetic braking due to mass loss and magnetic dipole radiation. For gravitational radiation to be emitted, the neutron star must have a quadrupole moment whose third time derivative $\dot{Q} \neq 0$. However, for reasonable estimates for $\dot{Q}$ it is unlikely that gravitational radiation would slow down the pulsar to periods ≥ 1 ms because it is most efficient at high frequencies⁸. For magnetic braking⁹⁻¹¹ to be effective requires that the Alfvén radius $r_A \equiv R(B^2 R / 2M\omega)^{1/2} > R$ where M is the rate of mass loss. For $B \approx 5 \times 10^8$ G this requires that $\dot{M} \leq 3 \times 10^{19}$ g s⁻¹. Hence, if the moment of inertia of the star is KMR^2 , with $K \sim 0.1$, the spin down time scale¹¹ is $\tau \sim K(\dot{M}/M)(2\omega_i M / B^2 R)^{2/5}$, where ω_i is the initial angular velocity of the pulsar. Hence we find $\tau \gg 2 \times 10^5$ yr. There is, however, no mechanism (such as vibrations, radiation pressure) which would maintain such a mass loss rate for so long. An extreme upper limit for $\dot{M}$ can be set by requiring that $\dot{M}V^2 \ll 4\pi R^2 \sigma T^4$ where T is the surface temperature of the neutron star and V the outflow velocity. At an age $\geq 10^5$ yr, one has $T \leq 10^5$ K so that if $V \sim 0.1c$ we have $\dot{M} \ll 10^9$ g s⁻¹. We thus deduce that $\tau \gg 10^{11}$ yr for magnetic braking. Magnetic dipole radiation is, however, more efficient and can brake the star to periods ≥ 1 ms on a time scale $\leq 10^8$ yr. Thus the age of the pulsar in our model

is $\leq 10^8$ yr but it is likely to be $\geq 10^4$ yr as there is no supernova remnant associated with it.

We next consider whether it is reasonable to expect a neutron star to be born with a field $\approx 5 \times 10^8$ G. Some insights may be gleaned by comparing pulsar magnetic fields with that of white dwarfs. Surveys⁷ of single white dwarfs show that only about 10% of them have detectable magnetic fields. Those that do, have fields $\sim 10^6$ – 10^8 G and hence have surface magnetic fluxes roughly comparable to that of most pulsars. Upper limits ranging from $\approx 5 \times 10^5$ G to $\sim 10^4$ G have been set for the non-magnetic white dwarfs. It is therefore plausible that some white dwarfs have magnetic fields $\sim 10^3$ G and have roughly the same surface flux as the fast pulsar. The range of magnetic fields of stars on the main sequence also spans at least 4 orders of magnitude. Thus unless there is a special mechanism which produces pulsars with magnetic fields in a narrow range $\sim 10^{11}$ – 10^{13} G one may expect that some pulsars, such as the fast pulsar, are formed with much weaker fields.

In our model we assume that the magnetic field of the fast pulsar has not decayed (see ref. 3) since birth. Let us examine whether this is plausible. The time scale for ohmic decay is much longer than the age of the Universe and therefore would not have taken place. Two other types of mechanism for field decay have been suggested, one dynamical¹² and the other due to MHD instabilities^{13–15}. The first takes place when the age of the pulsar is $\geq 10^6$ – 10^7 yr. However, this mechanism is unable to explain why the binary X-ray pulsar Her X-1 has a magnetic field¹⁶ $B \approx 5 \times 10^{12}$ G although its age according to evolutionary scenarios^{17,18} is $\approx 5 \times 10^8$ yr. The second mechanism leads to instabilities in cooling neutron stars provided they are not rotating too rapidly ($P \geq 1$ s) and hence does not apply to the fast pulsar.

Finally, we make the following predictions: (1) If the optical emission from the Crab and Vela pulsars is due to incoherent synchrotron radiation its optical luminosity¹⁹ $L \propto B^4 P^{-10}$. By comparison with the Crab pulsar it follows that the visual magnitude of the fast pulsar should be $m_v \sim 24 + (A_{\text{fast}} - A_{\text{Crab}})$ where A_{fast} , A_{Crab} are extinctions to the fast and Crab pulsars. (2) If the distribution of magnetic fields of neutron stars even remotely resembles that of white dwarfs or main-sequence stars, other pulsars with weak magnetic fields $\ll 10^{11}$ G are likely to be formed rotating rapidly. We may wonder why more of these have not been seen. We note, however, that the sensitivity of radio telescopes falls off drastically for periods ≤ 0.1 s, so that the paucity of such pulsars is not surprising. Thus, if our arguments are correct more pulsars with short periods are likely to be formed, although quantitative predictions are difficult because the distribution of magnetic fields of neutron stars at birth is not known. If on the other hand the fast pulsar was formed in a binary^{4,5}, few similar pulsars are likely to exist.

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Sunspot cycle and associated variation of the solar spectral irradiance

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Precise monitoring of the solar absorption-line spectrum in the period 1976–80 has revealed systematic changes of the strength of photospheric lines during the ascending part of the current solar cycle¹. The most likely cause is a slight cooling of the lower photosphere and a concomitant heating of higher layers. The total energy radiated into space thereby remains unchanged, in accordance with high-precision radiometry² covering the same period. Nevertheless, a flattening of the photospheric temperature gradient will be accompanied by a redistribution of energy in the solar spectrum. Its magnitude is predicted here using stellar model-atmosphere techniques. This 'change of colour' is characterized by a 0.2% decrease of the irradiance in the blue, and an increase of the same order in the red and near IR. In this way solar activity may modulate terrestrial climate even in the absence of perceptible changes of the solar constant.

Details of the observations and their analysis have been described in ref. 1. Absorption lines are sensitive probes of the physical state of the absorbing material, and are well-suited for long-term monitoring, being a relative, not absolute measurement. Long-term changes of solar temperature of a few kelvin, or changes of turbulent flow by 20 m s^{-1} will produce a signal well above the limit of detection of the 1976–80 data. After investigating possible instrumental and atmospheric effects it was found that over the first years of the current activity cycle the absorption lines have experienced a steady weakening, their equivalent widths having decreased by 0–3% depending on the line considered. The most likely explanation for this line weakening turned out to be a slight cooling of the lower photosphere, simultaneous with a concomitant slight heating of higher photospheric layers, by typically ± 10 to ± 20 K at those optical depths accessible to observations ($\tau_{5,000} \approx 2$). The total energy radiated into space, that is the effective temperature of the Sun and the solar constant remains unchanged in this model. This is in accordance with Active Cavity Radiometer observations² which impose an upper limit on long-term solar total irradiance variability of $\pm 0.1\%$ between 1976 and 1980.

Owing to the wavelength dependence of the absorption coefficient of photospheric matter, different wavelengths of the emerging radiation originate at different levels in the solar atmosphere. As a consequence the change of the photospheric

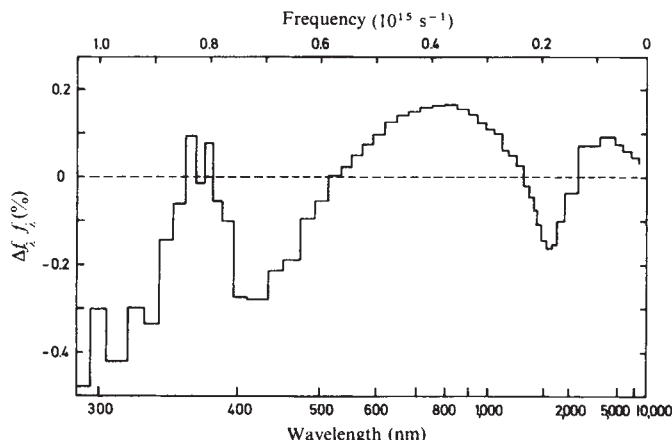


Fig. 1 Predicted variation of the solar spectral irradiance between 1976 and 1980.

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Table 1 Predicted variation Δf_λ of the solar spectral irradiance between 1976 and 1980

Wavelength (nm)	Δf_λ (erg s ⁻¹ cm ⁻² nm ⁻¹)	$\Delta f_\lambda/f_\lambda$ (%)	Wavelength (nm)	Δf_λ (erg s ⁻¹ cm ⁻² nm ⁻¹)	$\Delta f_\lambda/f_\lambda$ (%)
202.8	0.073	0.911	635.0	1.93	0.123
211.3	-0.120	-1.43	665.0	2.06	0.139
220.0	-0.147	-1.27	695.0	2.02	0.145
230.0	-0.052	-0.076	730.0	1.99	0.157
240.0	0.180	0.279	770.0	1.84	0.159
248.1	0.062	0.509	805.2	1.74	0.161
258.1	-0.594	-0.334	835.2	1.63	0.163
270.0	-3.13	-0.703	875.0	1.39	0.153
280.0	0.729	0.321	925.0	1.17	0.142
290.0	-3.05	-0.479	975.0	0.925	0.124
300.0	-1.31	-0.297	1,025.0	0.731	0.109
310.0	-4.03	-0.422	1,075.0	0.600	0.100
320.0	-2.91	-0.298	1,125.0	0.352	0.064
330.0	-4.08	-0.334	1,175.0	0.244	0.049
340.0	-1.59	-0.143	1,225.0	0.164	0.036
350.0	-0.712	-0.063	1,275.0	0.108	0.026
359.8	0.987	0.094	1,325.0	-0.081	-0.021
366.1	-0.194	-0.015	1,375.0	-0.162	-0.046
371.2	0.842	0.078	1,429.4	-0.246	-0.076
380.0	-0.649	-0.055	1,479.4	-0.325	-0.109
390.0	-1.20	-0.101	1,550.0	-0.380	-0.143
402.5	-4.39	-0.276	1,650.0	-0.367	-0.163
420.0	-5.04	-0.277	1,675.0	-0.327	-0.153
440.0	-4.06	-0.215	1,800.0	-0.168	-0.101
460.0	-3.80	-0.190	2,000.0	-0.026	-0.035
480.0	-1.86	-0.094	2,700.0	-0.0274	0.072
500.0	-1.06	-0.055	4,000.0	0.0078	0.092
520.0	0.163	0.009	5,000.0	0.0027	0.075
540.0	0.406	0.022	6,500.0	0.79×10^{-3}	0.061
560.0	0.864	0.048	10,000.0	0.11×10^{-3}	0.044
580.0	1.28	0.073	20,000.0	0.50×10^{-5}	0.033
605.0	1.63	0.097			

temperature gradient will give rise to a redistribution of energy in the spectrum. If the effective temperature of the Sun remains unchanged, as it does in our model, the total irradiance (integrated over all wavelengths) also remains constant. About 99% of the energy is radiated at wavelengths between 300 and 10,000 nm where the main absorption processes are well known: free-free and bound-free absorption of the negative hydrogen ion in the IR and visible part of the spectrum, and bound-bound absorption of various elements in the violet and near-UV. We have calculated the resulting change in the spectrum, using standard H^- data and taking line absorption into account with the distribution-function approximation³, in which the contribution of lines is averaged over suitably chosen wavelength intervals.

The results are shown in Table 1 and Fig. 1. In the wavelength range 200–20,000 nm fractional changes $\Delta f_\lambda/f_\lambda$ between -0.42% and +0.16% are predicted to have occurred. What counts for the energy balance is the absolute change Δf_λ rather than $\Delta f_\lambda/f_\lambda$. Since f_λ peaks around 500 nm and drops towards the UV and IR, the main feature is a slight 'reddening' of the light of the solar disk in the sense that the red brightens at the expense of the blue. This simply reflects the well-known wavelength dependence of H^- absorption, whose maximum near 850 nm coincides with that of $\Delta f_\lambda/f_\lambda$. The variation with wavelength becomes irregular towards the UV because of the rapidly varying contribution of absorption lines. Below 200 nm chromospheric radiation becomes increasingly important. The solar spectrum is known to exhibit a pronounced solar-cycle modulation there, amounting to a factor of two near 140 nm (refs 4, 5). Energetically, however, these variations are negligibly small compared with those at the longer wavelength considered here.

Any such redistribution of energy in the solar spectrum will affect the thermal structure of the Earth's atmosphere, in particular of the troposphere^{6,7}. Detailed modelling will be required to evaluate this response and the associated climatic change. An important factor will be the fraction of solar radiation that

is transmitted by the atmosphere and reaches the Earth's surface. This radiation is carried mainly in the long-wavelength part of the visible and in the near IR where, according to our model, significant ($\geq 0.1\%$) changes can occur during a solar cycle.

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Long-lived eddies in the laboratory and in the atmospheres of Jupiter and Saturn

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The Great Red Spot (GRS), the three White Ovals, and other long-lived anticyclonic eddies in Jupiter's atmosphere might be dynamically similar¹ to the closed, stable baroclinic eddies that were first discovered in laboratory studies of thermal convection in a rotating fluid subject to internal heating and sidewall cooling^{2,3}. We outline here results of new laboratory and numerical experiments on the structure, energetics and stability of such eddies, which strongly support the suggestion that these laboratory and atmospheric flows (including similar eddies

found on Saturn⁴) might all be manifestations of the same dynamical process—'sloping' or 'slantwise' convection. Included in our numerical experiments are cases with internal cooling and sidewall heating, in which stable baroclinic eddies with a cyclonic peripheral jet stream at upper levels surrounding a region of slow descent have been produced and studied. We suggest that these cyclonic eddies are dynamically similar to the 'barges' observed in Jupiter's Tropical and Temperate Belts⁵.

The atmospheres of Jupiter and Saturn exhibit a variety of large-scale eddies, prominent at the level of the upper clouds, some of which have relatively long lifetimes, from months to many years. The best known examples on Jupiter are the GRS, discovered in the seventeenth century, and the three White Ovals, which formed in 1939 in the aftermath of the South Tropical Disturbance. Image data from the recent Voyager fly-by missions have added considerably to the number of long-lived atmospheric eddies identified on both Jupiter and Saturn, including the 'B-spots' and 'barges'^{4,6-8}.

Suggestions as to the nature of the GRS and other long-lived eddies have been reviewed elsewhere⁹⁻¹². The work closest to that presented here is that of Williams¹³, who produced latitudinal (E-W) jet streams and transient baroclinic eddies in integrations of a numerical model similar to those used to investigate mid-latitude flow in the Earth's atmosphere. Baroclinic eddies obtain their kinetic energy mainly by the direct conversion of available potential energy, due to the action of gravity on horizontal density variations maintained by impressed differential heating and cooling, through the mechanism of 'slantwise convection', the incipient behaviour (but not the fully-developed properties) of which are described by the theory of baroclinic instability¹⁴.

Laboratory experiments on slantwise thermal convection in a cylindrical fluid annulus, which rotates about its vertical axis of symmetry and is subject to differential heating and cooling in the horizontal, have provided considerable insight into the properties of fully-developed large-scale baroclinic disturbances in the atmospheres of the Earth and other planets¹⁵. The general character of the flow depends on the imposed experimental conditions and may be either axisymmetric, analogous to the Hadley-type flow invoked in theories of the circulation of the Earth's tropical atmosphere, or non-axisymmetric, owing to the presence of large-amplitude baroclinic disturbances associated with large-scale slantwise convection. Depending on the precise conditions, these baroclinic disturbances may exhibit either 'regular' or 'irregular' spatial and temporal characteristics. Regular flows either persist indefinitely without change of form, or they exhibit a periodic 'vacillation' in amplitude or shape; irregular flows exhibit aperiodic spatial and temporal

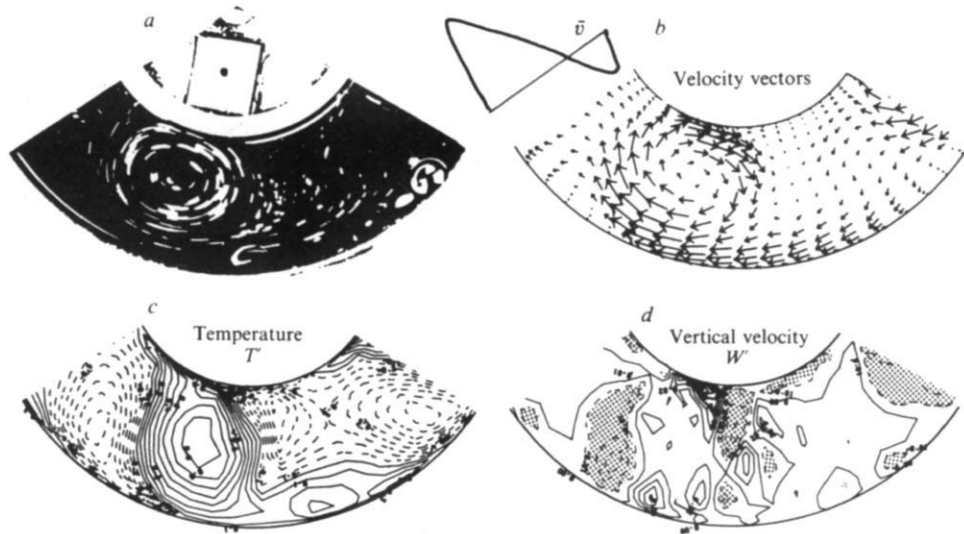
variations, reminiscent of mid-latitude flow in the Earth's atmosphere.

The detailed structure of the baroclinic disturbances and their associated background flow depends largely on the distribution of heating and cooling^{1,2}. This was varied by Hide and Mason² using apparatus in which the fluid was heated internally, by passing an alternating electric current through it, and cooled using one or both sidewalls. When substantial cooling was effected at both sidewalls so that the impressed temperature gradient changed sign near mid-radius and the density there was a minimum (since the coefficient of cubical expansion α was positive), closed anticyclonic eddies embedded in an anticyclonic background azimuthal flow were almost the sole features at upper levels. This pattern of horizontal motion strongly resembles the measured flow around the GRS and White Ovals on Jupiter. Accordingly, it was suggested¹ that the long-lived eddies might be manifestations of slantwise convection within the banded structure of Jupiter's atmospheric circulation, with the eddies serving to transfer heat from the deeper middle parts towards the upper edges of the zones in which they occur.

We now examine this suggestion by improving and extending the laboratory experiments of Hide and Mason and conducting associated numerical studies. The numerical model is used here primarily to obtain detailed information on the flow structure and energetics, which are difficult to study in the laboratory, and the laboratory experiments verify the numerical results and establish the range of conditions in which various types of flow occur. Our apparatus was similar to that used by Hide and Mason, and a detailed description will be given elsewhere. The numerical experiments were carried out using an adaptation of a model developed¹⁶ for integrating the Navier-Stokes equations for a Boussinesq fluid in cylindrical annular geometry, with the addition of an internal heat source of intensity proportional to the inverse square of the distance from the axis.

The upper level flow for a typical experiment with internal heating, sidewall cooling and a stress-free upper surface, is shown in Fig. 1, which illustrates the numerical simulation of a steady regular flow in the same conditions as one of the laboratory experiments of Hide and Mason. The dominant feature is a regular series of anticyclonic eddies, in which the horizontal motion is concentrated into a closed peripheral jet-stream near the edge of each eddy. A meandering jet-stream encloses the pattern of eddies, the strength of which, relative to the motion in the eddies, depends largely on the ratio of the rates at which heat is withdrawn at the inner and outer sidewall respectively². The horizontal motions in the eddies advect heat from the main body of the fluid towards the inner and outer sidewalls, and the vertical motions advect heat upwards, thereby

Fig. 1 Numerical simulation of flow in an internally heated rotating annulus of fluid with sidewall cooling and a stress-free upper surface, corresponding to a laboratory experiment of Hide and Mason² with regular wave number 4: *a*, top surface streak photograph from the laboratory experiment; *b*, horizontal velocity vectors near the upper surface of the simulated flow (the inset shows the profile of azimuthally-averaged zonal velocity $\bar{v}$); *c*, perturbation temperature field (after subtraction of azimuthal average) near the top surface of the simulated flow (contour interval = 0.1 °C); *d*, perturbation vertical velocity field (after subtraction of azimuthal average) just below the upper surface of the simulated flow (contour interval = 0.01 cm s⁻¹, and hatched regions indicate descending motion exceeding -0.01 cm s⁻¹). All negative contours are dashed.



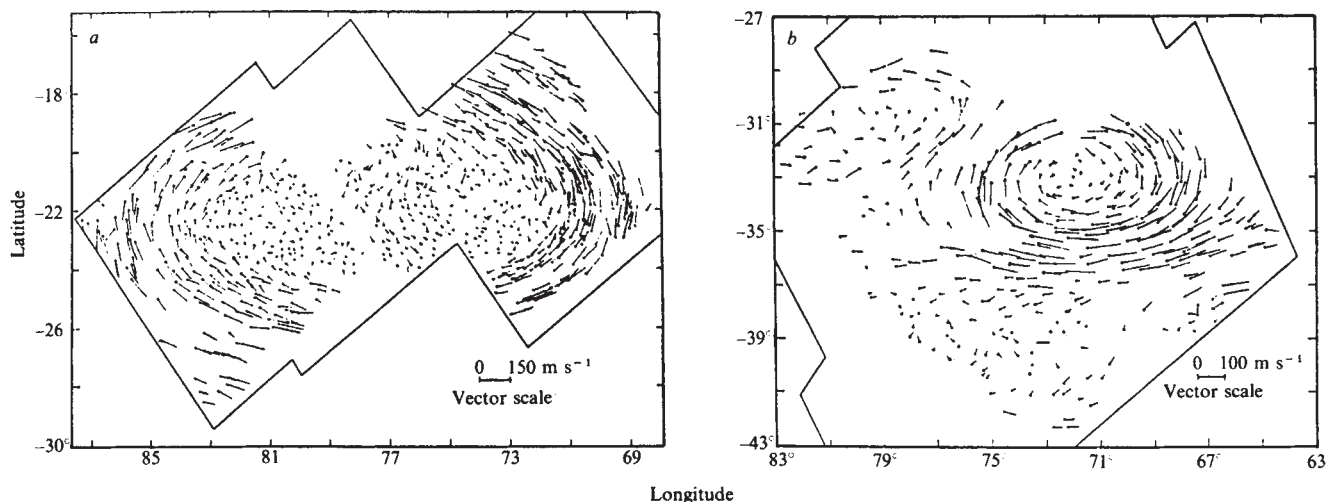


Fig. 2 Vector representation of the horizontal flow fields around: *a*, the Great Red Spot; *b*, one of the White Ovals, in the southern hemisphere of Jupiter, derived from Voyager data by Mitchell *et al.*²¹. The small dark circle at the end of each vector indicates the initial position of each cloud tracer used in the analysis, and the tail of each points downwind.

generating and maintaining a stable density gradient in the vertical. In the absence of dispersive effects, the eddies drift slowly relative to the apparatus at a speed close to the volume-averaged azimuthal flow which, in the case shown here, is relatively weak and retrograde. The eddies themselves are largely quasi-geostrophic, warm-cored high pressure disturbances with upward motion near the centre. The ratio of the horizontal scale L to the vertical scale D of the eddies satisfies the usual relationship for quasi-geostrophic flow in a stably-stratified fluid:

$$L/D \approx N/f \quad (1)$$

where

$$N = [g \partial(\ln \theta) / \partial z]^{1/2} \quad (2)$$

is the Brunt-Väisälä frequency, a measure of the static stability if θ denotes the potential temperature and z height, and f is the vertical component of the basic rotation vector (the quantities N and D are not well determined for Jupiter or Saturn, but values of ND ($\approx fL \approx 10^{-4} \times 10^7 = 10^3 \text{ ms}^{-1}$) consistent with Hide's¹ hypothesis that the GRS and other long-lived anticyclonic eddies are produced by sloping convection are not incompatible with the available evidence). Associated strong ageostrophic effects in the laboratory flows are concentrated in the peripheral jet-stream of each eddy, where the relative

acceleration of a typical individual fluid element is comparable with Coriolis accelerations, as well as in boundary layers, where viscous effects are important.

These eddies bear a marked resemblance in their background mean flow and in their thermal and horizontal velocity fields to the jovian features discussed above (see Fig. 2) and to similar atmospheric eddies found on Saturn⁴. Detailed analyses of the 'Voyager' image data indicate that many of the long-lived oval atmospheric eddies, including the GRS and the White Ovals, have several important features in common, notably cloud texture and colour^{17,18}, the morphology of their thermal (IR) fields^{19,20}, horizontal velocity fields²¹, and the form of the zonally-averaged background flow, implying that they could all be manifestations of the same dynamical process. Most oval eddies occur in the anticyclonic background flow between two oppositely-directed zonal jets which, according to the thermal wind equation, could be associated with the underlying thermal contrasts between the alternating light and dark cloud bands^{9,22}, the light cloud bands corresponding to warmer zonal mean temperatures on a geopotential surface than at adjacent latitudes. The eddies themselves are anticyclonic features (at the upper cloud level), in which the horizontal motion is largely geostrophic and concentrated into a re-circulating jet-stream at the periphery of each eddy²¹ (see Fig. 2). The eddy core is a warm and relatively quiescent high pressure region in which

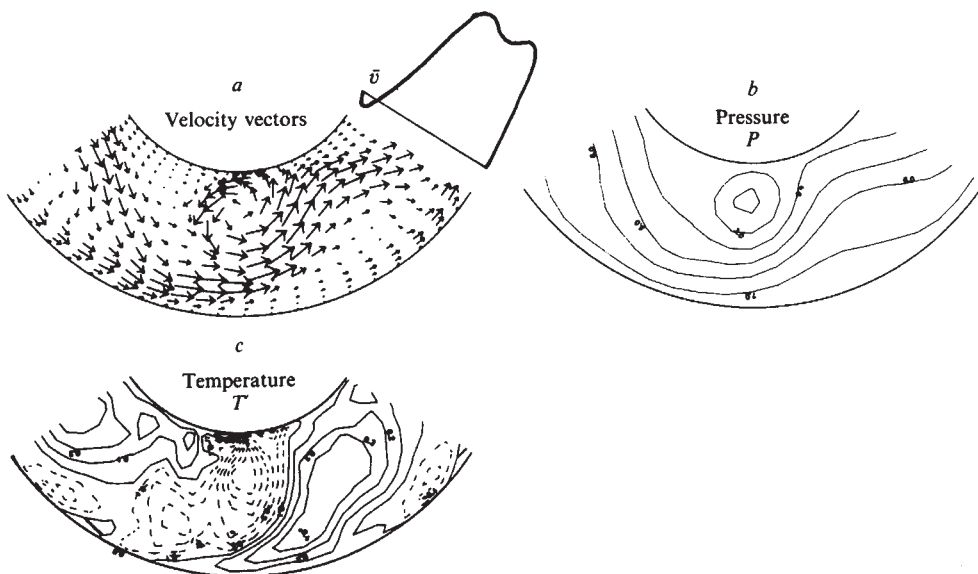


Fig. 3 Numerical simulation of the flow in an internally cooled rotating annulus of fluid with sidewall heating, subject to the same boundary conditions and equal and opposite (negative) internal heating as the flow illustrated in Fig. 1: *a*, horizontal velocity vectors near the upper surface (the inset shows the profile of azimuthally-averaged zonal velocity $\bar{v}$); *b*, kinetic pressure field near the upper surface (contour interval = $1 \text{ cm}^2 \text{ s}^{-2}$); *c*, perturbation temperature field (after subtraction of azimuthal average) near the upper surface (contour interval, 0.1°C). All negative contours are dashed.

slow upward motion may occur. The oval eddies appear superficially to be isolated features, but many occur, like the laboratory eddies, at almost regular intervals in longitude interspersed with weak cyclonic regions⁸. Surrounding the peripheral jet-stream of each eddy in our model is a narrow region of downward motion (see Fig. 1d), which forms the descending branch of the overturning circulation associated with the ageostrophic motion in the jet-stream. Such a feature does not depend primarily on the presence of the sidewalls of the apparatus, but results largely from the non-linear frontogenetic development of the eddy. Thus it could account for the 'collar' of IR emission observed to surround the GRS^{19,23} (and possibly the White Ovals²⁰), and attributable to the absence of high-level cloud in regions of sinking motion.

All these laboratory results concern a system in which the horizontal temperature gradient changes sign, with the mean temperature on a level surface reaching a maximum near mid-radius, the corresponding density for a fluid of positive α being a minimum. Also of interest is the complementary system in which the impressed differential heating is the same but α is negative (as in the case of water between 0 and 4°C) or, alternatively, α remains positive and the horizontal temperature gradient changes sign but with a temperature minimum near mid-radius, as would obtain when the fluid is cooled internally and heated at the sidewalls. Because investigating such a system in the laboratory presents certain practical difficulties we used our numerical model for this purpose. As expected on theoretical grounds^{1,2}, closed cyclonic eddies were found at upper levels in the regular flow regime, embedded in a cyclonic background azimuthal flow (see Fig. 3). The horizontal motion in each eddy is concentrated into a compact cyclonic peripheral jet-stream, and a continuous meandering jet-stream encloses the pattern. Each eddy is a relatively cool, quasi-geostrophic low pressure disturbance with slow descending motion at its centre. In this case, the horizontal motion in the eddies serves to transfer heat into the main body of the fluid.

In applying these results to the atmospheres of Jupiter and Saturn in a similar manner to the internally heated system discussed above, we would expect that long-lived cyclonic eddies with peripheral jet-streams might occur where the shear of the background azimuthal flow is cyclonic, suggesting from the thermal wind equation that the mean (with respect to longitude) temperature of a geopotential surface is less than at adjacent latitudes. Such conditions may prevail on Jupiter between the zonal jets associated with the Tropical and Temperate Belts²². Possible candidate features for comparison with the laboratory cyclonic eddies include the 'barges', the relatively long-lived brown oval spots which occur on Jupiter in regions of cyclonic background shear around 14°N. They are cyclonic features with a peripheral jet-stream apparently surrounding a cool-cored low pressure region associated with high IR brightness temperatures, indicating an absence of high level clouds in a region of slow sinking motion⁵. The 'barges' may also, therefore, be manifestations of quasi-steady slantwise convection, serving to advect heat within the belts in which they occur, from the edges at low levels towards the central regions at high levels. The ascending branch of the overturning circulation associated with ageostrophic motions in the peripheral jet-stream would manifest itself as a narrow 'collar' of high cloud associated with comparatively weak IR emission. The detection of such features will require observations with high spatial resolution.

In promoting the hypothesis that many of the long-lived eddies on Jupiter and Saturn are manifestations of quasi-steady slantwise convection within the latitudinal belts and zones, we argue that many of the results of laboratory experiments on flow regimes, structure and stability may apply (albeit qualitatively) to any rotating fluid system with essentially similar (mainly geostrophic) background thermal and velocity fields. The laboratory experiments demonstrate that long-lived baroclinic eddies can exist over a wide range of conditions (including those likely to prevail in the atmospheres of Jupiter and Saturn).

The various regimes of flow found in the laboratory experiments (axisymmetric, regular and irregular) are now known to be typical of a wide range of non-linear dynamical systems²⁴. In particular, the regular regime of thermal convection in a rotating fluid annulus is not to be regarded as a special phenomenon, dependent for its existence on the geometry and size of the system.^{2,25} There is abundant experimental evidence that regular flows do not owe their existence primarily to the action of strong viscous effects or to the absence of dispersive effects²⁶ which, in a planetary atmosphere, would be associated with the latitudinal variation of the Coriolis parameter. Viscosity and dispersive effects modify the eddies in certain details, but they do not affect their main properties and stability which are primarily due to the effects of nonlinear advection. This is why it is possible to simulate in the laboratory large-scale dynamical processes in planetary atmospheres.

Numerous questions remain, of course, concerning the precise modifying influence of dispersive effects and atmospheric compressibility, and the isolated nature of the long-lived atmospheric eddies. The latter might be due to the influence of the eddies themselves on the thermal and mechanical boundary conditions effectively prevailing at the edges of the atmospheric latitudinal bands.* The origin of the atmospheric banded structure of Jupiter and Saturn must also be considered in greater detail. The present work does not account for the atmospheric bands, but merely establishes the properties of slantwise convection in the presence of a similar background flow. While the resolution of many of these questions may require more detailed observations of Jupiter and Saturn and further analyses of existing observations, insight may be gained from laboratory and numerical experiments on effects produced by sloping the endwalls (thereby introducing dispersion into the flow²⁶), and by reducing viscous effects still further so as to investigate the small-scale shear instabilities that develop on the jet-stream when the local Reynolds number is sufficiently high. Such work is now in progress and will be reported elsewhere.

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Note added in proof: In connection with the isolated nature of the eddies,* it has now been found, using the above-mentioned laboratory apparatus, that a long-lived isolated closed eddy can readily be produced within the regular non-axisymmetric flow regime under conditions close to the transition to axisymmetric flow.

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¹⁸⁷Re–¹⁸⁷Os systematics in meteorites and cosmochemical consequences

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A new technique based on isotope dilution¹ has allowed the reappraisal of ¹⁸⁷Re–¹⁸⁷Os isotopic tracers^{2,3}. Rhenium and osmium were chemically separated and their isotopic compositions determined by ion-microprobe mass spectrometry. Such an approach led to the absolute dating of meteorites¹ and allowed us to estimate the evolution of the Os isotopic composition in the Earth's mantle⁴. Having improved the analytical procedure and recalibrated our osmium spike, we found that the value we had used previously¹ was too high by a few per cent. We therefore include here our eight previous results on iron meteorites and on St Severin, corrected for this change in spike calibration. Our data now include 11 analyses on irons, and the iron phases of 10 chondrites and of one mesosiderite. From these data we propose a revised and more precise value for the rhenium decay constant, together with a new estimate for the age of the Galaxy.

The chemical procedure to separate Os and Re is basically that described in ref. 1: the concentrations are determined through the isotope dilution technique and the isotopic measurements are done in an ion-bombardment mass spectrometer (Cameca ion microprobe)^{5,6}. However, several modifications have been made to improve the sensitivity of the measurements on the ion probe. In particular the sample holder has been changed from pure aluminium to pure, polished silicon plates. After loading as the hexachloro-osmate salt, the sample is heated to ~1,000 °C under a primary vacuum of 10^{–3} torr and the salt is thus decomposed into the metal. This procedure has two major advantages: part of the organic matter is decomposed, which reduces the hydrocarbon mass interferences; and the stability of the signal and the ionization yield are improved when oxygen pressure around the sample (usually 10^{–7} torr) is brought up to 10^{–5} torr. The hydride interferences are also lowered in these conditions.

Englert and Herpers⁷ have pointed out that the isotopic ¹⁸⁷Os/¹⁸⁶Os ratio is related to the type of ore from which the osmium has been extracted. This relationship concerns only the 187 isotope, all other isotopes being stable. It is, therefore, important to determine not only this (187/186) ratio but also several isotope ratios which serve us as normalization values used for some hydride corrections.

The isotopic composition of osmium proposed by Nier⁸ is:

184	186	187	188	189	190	192
0.02	1.59	1.61	13.3	16.1	26.4	41.0 %

(total 100.02%)

This leads, for example, to the following isotopic ratios (as normalized to the ¹⁸⁸Os):

184/188	0.0015		
186/188	0.11955	187/188	0.12105
189/188	1.2105		
190/188	1.9850		
192/188	3.08271		

Taking the (192/188) ratio as an internal standard (3.08271) we found for our Merck standard the following values:

184/188	0.0018 ± 0.0002		
186/188	0.12045 ± 0.00007	187/188	0.11367 ± 0.00007
189/188	1.2232 ± 0.0004		
190/188	1.9847 ± 0.0008		

Mass fractionation correction was computed using a linear law. Although our sample is less radiogenic than Nier's, the important result is that slightly different and more precise isotope measurements have been obtained for the whole spectrum. Of course, these values might be fractionated with respect to the 'true' values: the (198/188 = 3.08271) reference is arbitrary as no separate absolute determination is available (whereas there is one for Re)⁹. All (¹⁸⁷Re/¹⁸⁶Os) and (¹⁸⁷Os/¹⁸⁶Os) ratios given here (including those previously¹ reported) are now normalized to a (¹⁸⁶Os/¹⁸⁸Os) ratio of 0.12035, while the results were normalized to (¹⁸⁶Os/¹⁸⁸Os) = 0.11955 in ref. 1.

More detailed measurements have shown that the concentration of our ¹⁹⁰Os spike (4.83 µg per g as determined at the time of calibration) was actually 4.55 µg per g when analysing the samples. This difference was essentially due to the difficulty of obtaining complete isotopic homogenization in the process of isotope dilution: this was attributed to a progressive change in the chemical form (OsO₄ → OsO₃N[–]) under which our osmium spike was stored in aqueous solution¹⁰. That this slight change had affected the earlier results¹ was shown by making duplicate analysis of two samples (Coahuila and Canyon Diablo). Therefore, taking into account these adjustments, the value of λ_{Re} computed on the basis of the six samples previously analysed¹ should have been: 1.53 ± 0.08 × 10^{–11} yr^{–1} instead of the previously proposed 1.62 ± 0.08 × 10^{–11} yr^{–1}.

Several new meteorites—irons and iron phase of chondrites—have since been analysed and our whole set of data is given in Table 1. Note that the analysis of the Tocopilla meteorite has almost doubled the spread in Re/Os ratio relative to our previous range¹. All samples fall remarkably well on a single straight line (Fig. 1), indicating that they all formed simultaneously within a time span of roughly 90 Myr from an isotopically homogenized primordial source (regarding Os). The points

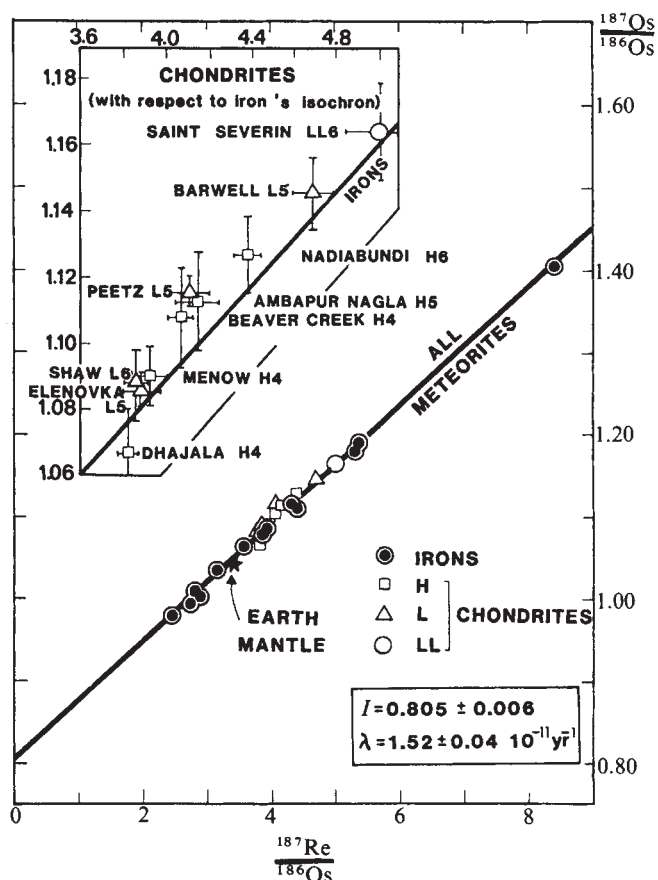


Fig. 1 ¹⁸⁷Re/¹⁸⁶Os diagram for seven irons and one mesosiderite (this work and ref. 1). λ_{Re} has been calculated on the basis of an age of 4,550 Myr and is indistinguishable from the 'all meteorites' value (1.50 and 1.52 respectively).

Table 1 Re and Os concentrations and Os isotopic composition in several iron meteorites and metallic phase of chondrites

			Re	Os			Literature data*	
			(p.p.m.)	(p.p.m.)	$^{187}\text{Re}/^{186}\text{Os}$	$^{187}\text{Os}/^{186}\text{Os}$	Re	Os
							(p.p.m.)	
Iron meteorites								
Tlacotepec	(1)	IVB	3.28±0.03	53.7±0.4	2.46±0.03	0.980±0.004	3.0	39
	(2)		3.69±0.03	54.4±0.7	2.73±0.05	0.994±0.006		
	(3)		3.69±0.03	52.8±0.6	2.81±0.05	1.008±0.006		
Canyon Diablo	(1)	IA	0.247±0.001	2.30±0.02	4.33±0.08	1.115±0.003	0.22	2.3
	(2)		0.222±0.002	2.03±0.02	4.40±0.06	1.113±0.006		
Coahuila	(1)	IIA	1.40±0.01	10.5±0.06	5.36±0.07	1.187±0.011	1.3	6.0
	(2)		1.42±0.01	10.7±0.07	5.34±0.05	1.182±0.005		
Tocopilla		IIA	0.222±0.02	1.06±0.01	8.42±0.15	1.404±0.006	0.25	1.3
Casas Grandes		IIIA	0.731±0.006	9.30±0.14	3.16±0.07	1.035±0.005	0.45	3.2
Henbury		IIIA	1.53±0.06	15.9±0.2	3.87±0.16	1.080±0.004	0.73	2.3
Charcas		IIIA	1.15±0.04	16.1±0.5	2.87±0.17	1.004±0.009	0.13	1.10
Mt Edith		IIIA	≤0.001	~0.01				
Mesosiderite								
Estherville			0.472±0.005	5.29±0.05	3.59±0.09	1.063±0.05		
Chondrites (metal)								
Dhajala		H3	0.264±0.001	2.78±0.02	3.82±0.04	1.067±0.013	0.5	5
Menow		H4	0.275±0.003	2.81±0.03	3.92±0.09	1.090±0.006		
Beaver Creek		H4	0.307±0.001	3.03±0.03	4.07±0.05	1.108±0.010		
Nadiabundi		H5	0.206±0.001	1.89±0.02	4.38±0.06	1.127±0.005		
Ambapur Nagla		H5	0.342±0.003	3.32±0.05	4.14±0.10	1.113±0.008		
Peeetz		L5	0.413±0.004	4.04±0.04	4.11±0.09	1.115±0.004	0.6	6
Elenovka		L5	0.588±0.003	6.09±0.06	3.88±0.09	1.086±0.004		
Barwell		L5	0.499±0.003	4.28±0.06	4.69±0.09	1.146±0.009		
Shaw		L6	0.221±0.001	2.30±0.02	3.86±0.05	1.088±0.008		
St Severin		LL6	0.939±0.008	7.55±0.18	5.00±0.16	1.164±0.015		

* References are indicated in the text.

define a very good isochron in the ($^{187}\text{Os}/^{186}\text{Os}$) versus ($^{187}\text{Re}/^{186}\text{Os}$) diagram, with an initial ratio of ($^{187}\text{Os}/^{186}\text{Os}$) = 0.807 ± 0.006 . This value is indistinguishable from the previous¹ one (0.805 ± 0.011) but is twice as accurate, due to the greater range in Re/Os values.

The iron phase of the Estherville mesosiderite plots exactly on the isochron defined by the iron meteorites (Fig. 1), indicating that this meteorite formed within a period of ~ 100 Myr simultaneously with the iron meteorites. This is the first precise determination on this type of meteorite. With $\lambda_{\text{Re}} = 1.53 \times 10^{-11} \text{ yr}^{-1}$, its age of $4,250 \pm 50$ Myr is consistent with the value proposed by Murthy *et al.*¹¹ from Rb-Sr measurements on the silicate fraction ($4,350 \pm 100$ Myr). According to these authors, the younger age could be due to either a very slow cooling of the parent body or a specific disturbance of the Rb-Sr system in this type of object. Both explanations are consistent with the solar Re-Os age as the refractory Re-Os system might be

expected to be less sensitive to temperature or shock effects than the Rb-Sr system.

As Re and Os are strongly siderophilic, they are concentrated in the metal phase of meteorites, as was shown extensively by the analyses of both elements^{12,13} in various meteorites of different groups (H, L, LL).

Therefore, we analysed, as we did previously¹ for St Severin (LL6), magnetic separates from chondrites of various groups (H, L, LL) and various petrological types³⁻⁵.

The points representing the chondrites also plot on the isochron defined by the iron meteorites, or slightly above the line (Fig. 2), but the error bars (2σ) just overlap it, except for Peeetz. The difference of ~ 70 Myr found between the iron-meteorite isochron and the line joining the initial of that isochron to the mean point of all chondrites is smaller than the combined uncertainties on the two lines. The slopes and initials of the irons and chondrites best fit lines (σ -weighted) overlap each other:

	Slope	Initial
Irons	0.0706 ± 0.0014	0.807 ± 0.006
Chondrites	0.0747 ± 0.0060	0.800 ± 0.024

The Re-Os data indicate that it is premature to propose a significant difference between the formation of iron meteorites and chondrites.

As most chondrites plot on the iron-meteorite isochron, and considering the consistency between the ages of chondrites derived from Rb-Sr studies, our results are not inconsistent with a formation interval for irons and chondrites of 30 Myr as inferred by ^{129}I - ^{129}Xe chronology^{14,15}. Assuming a common age of 4,550 Myr for all these meteorites, we may now propose a slightly revised and more precise value for the ^{187}Re decay constant: $\lambda_{\text{Re}} = 1.52 \pm 0.04 \times 10^{-11} \text{ yr}^{-1}$. Note that the value of the initial ($^{187}\text{Os}/^{186}\text{Os}$) ratio for all meteorites is identical to that defined by the iron meteorites only.

The iron meteorites have extremely variable Re and Os contents: the groups IIA, IIIA and IVB show refractory siderophilic element enrichments, group IVB being exceptional in this respect. Note that for some samples, particularly those from group IIIA, our values are very different from those found

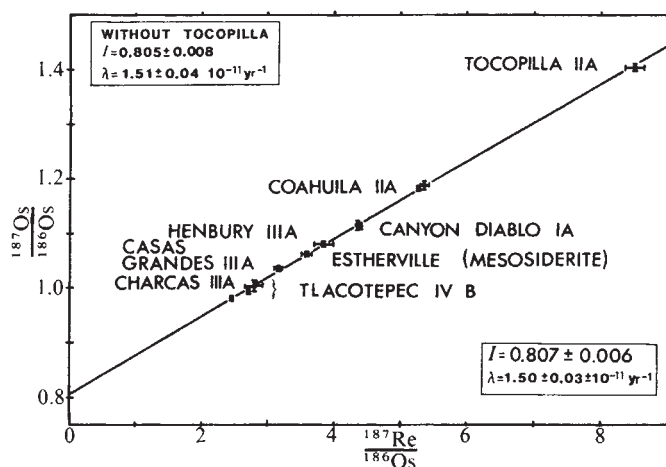


Fig. 2 $^{187}\text{Re}/^{186}\text{Os}$ diagram for all meteorites studied in this work and in ref. 1. λ_{Re} value is for $T = 4,550$ Myr. Positions of chondrites relative to iron's isochron (from Fig. 1) are indicated in the upper part of the diagram. All samples—except Peeetz—plot on the line within their error bars (2σ).

Table 2 Re and Os isotopic compositions of standard and IVB iron meteorite Hoba

Isotopes	Standard	Hoba
$^{185}\text{Rh}/^{187}\text{Re}$	0.608 ± 0.003	0.607 ± 0.003
$^{184}\text{Os}/^{188}\text{Os}$	0.0018 ± 0.0002	0.0016 ± 0.0004
$^{186}\text{Os}/^{188}\text{Os}$	0.12035 ± 0.00007	0.1202 ± 0.0002
$^{187}\text{Os}/^{188}\text{Os}$	0.11367 ± 0.00007	0.1215 ± 0.0004
$^{189}\text{Os}/^{188}\text{Os}$	1.2232 ± 0.0004	1.221 ± 0.002
$^{190}\text{Os}/^{188}\text{Os}$	1.9847 ± 0.0008	1.985 ± 0.005
$^{192}\text{Os}/^{188}\text{Os}^*$	3.08271	3.08271

* Normalization ratio.

in the literature (see ref. 16 for a compilation) for both absolute and relative abundances of the elements (see Table 1).

The closeness of our duplicate analyses to bibliographical data¹⁶ for Canyon Diablo seems to indicate a fairly homogeneous meteorite. Our Coahuila sample, however, although very homogeneous, differs significantly from the literature data¹⁶ in terms of both absolute and relative abundances. A possible explanation could be, of course, the presence of big heterogeneities within IIIA samples. Note that the literature data were obtained by activation analysis while our data are measured by isotope dilution mass spectrometry.

H, L and LL chondrites show remarkably grouped Re and Os contents, considering both literature data^{15,17} and our own. Also they show a much narrower range for the ($^{187}\text{Re}/^{186}\text{Os}$) values which actually cluster well above the 'mean solar' value (~ 2.82) derived from CI meteorite Orgueil. This surprising feature has already been reported¹⁷ and no clear explanation has been provided. We might note that, of all the analysed meteorites, Tlacotepec (IVB) is the closest to this solar value: one might eventually relate this feature to the high temperature condensation that has been proposed^{18,19} to explain the refractory-volatile fractionation pattern specific to that group of meteorites; in fact, Re and Os would be among the very first elements to condense from the solar nebula.

Using the evolution curve of the ($^{187}\text{Os}/^{186}\text{Os}$) ratio in the Earth's mantle throughout time, we may determine the value of this ratio for today, and the ($^{187}\text{Re}/^{186}\text{Os}$) for the Earth's mantle. These values are 1.040 ± 0.010 and 3.34 ± 0.14 (with $\lambda_{\text{Re}} = 1.52 \times 10^{-11} \text{ yr}^{-1}$). The corresponding point plots well on the meteorite isochron defined above (see Fig. 2) but below the 'chondritic' domain.

Assuming a chondritic Earth model, such a position indicates an early differentiation of the core and, by mass balance, suggests that the Earth's core is similar to the IIA iron meteorites which are those plotting above the chondrite domain.

However, our analyses of chondrites were performed on the magnetic phase only, and the above reasoning admits that such a phase contains most of the Re and Os of the meteorite, which may be true if considering Prior's rule, but may also be wrong.

The IVB iron meteorites are very peculiar in their Re and Os contents. Because of their specific volatile-refractory fractionation, and because isotopic excesses of ^{107}Ag due to the decay of ^{108}Pd have recently been observed in some of those meteorites^{20,21}, several authors regard them as possible direct condensates from the solar nebula or supernova envelope^{19,20}.

If isotopic heterogeneities of various kinds—due to short-lived nuclides or nuclides of extra-solar origin—were present at the beginning of the condensation-accretion sequence, these IVB objects could have retained these 'anomalous' compositions. The nickel isotopic composition has been shown²² to be 'terrestrial' in several IVB irons (Hoba, Weaver Mountains, Cape of Good Hope). Although no osmium isotopic anomaly in meteorites has yet been reported²³, we have analysed some rhenium and osmium isotopic compositions. Data for Hoba are presented in Table 2 and indicate that these compositions are also terrestrial (with the exception of radiogenic ^{187}Os) within our analytical uncertainties: $\sim 0.5\%$ for Re and $0.2\text{--}0.3\%$ for Os.

Following our previous approach¹ after Clayton²⁴, and using the new λ_{Re} and initial ($^{187}\text{Os}/^{186}\text{Os}$) values, and also the new cross-section values for ^{186}Os and ^{187}Os (ref. 25), we may compute limits to the age of the Galaxy corresponding to the extreme cases of sudden and steady state nucleosynthesis respectively: $10,600 < T_{\text{Gal}} < 16,800 \text{ Myr}$. The change in the λ_{Re} value alone would yield a T_{Gal} decrease of roughly 800 Myr only. As Tinsley²⁶ pointed out recently, the major change comes from the new ($\sigma^{186}/\sigma^{187}$) cross-section ratio proposed by R. R. Winter and co-workers (ORNL, cited in ref. 25).

P. Pellas provided magnetic separates of Charcas, Nadiabundi, Elenovka, Barwell and Ambapur Nagla. The other magnetic separates were obtained from E. Olsen (Menow), C. B. Moore (Peetz), T. Kirsten (Shaw) and K. Marti (Dhajala). We also thank W. Herr for a Tocopilla sample and P. Hutchison for Beaver Creek, Henbury and Tlacotepec.

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¹⁵²Eu in samples exposed to the nuclear explosions at Hiroshima and Nagasaki

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Low background γ -ray spectrometry and neutron activation analysis were carried out on samples, such as roof tile and rock, that were exposed to the nuclear explosions in Hiroshima and Nagasaki, to determine the specific radioactivities of residual neutron-induced radionuclides such as ^{152}Eu which was found first by *in situ* γ -ray spectrometry in Hiroshima¹. The results reported here show that the variation of the apparent thermal neutron fluence with the slant distance from the explosion point, or air-zero point, of the nuclear weapon can be estimated even today in Hiroshima and Nagasaki. This makes it possible to re-evaluate the space radiation doses due to the nuclear explosions in both cities.

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In 1976, when *in situ* measurements of environmental radioactivity in the Hiroshima district were carried out using a high resolution portable Ge(Li) γ -ray spectrometer, low-level γ -ray peaks of ^{152}Eu were found¹ in a spectrum of a sample of material exposed to the 1945 nuclear explosion. The ^{152}Eu was considered to be a product of a neutron capture reaction between ^{151}Eu , a minor constituent in ordinary rock, brick and the like, and neutrons released during the explosion. This assumption was based on the fact that ^{151}Eu , of which natural isotopic abundance is 47.9%, has an extremely large thermal neutron capture cross-section of $5.8 \times 10^{-21} \text{ cm}^2$ and that the half life of ^{152}Eu is a moderately long one (13.2 yr).

To confirm the correlation between the specific radioactivity of ^{152}Eu and the slant distance from the explosion point of the nuclear weapon, samples such as roof tiles, bricks and rocks which must have been exposed to the nuclear explosions were collected from sites in Hiroshima and Nagasaki. The locations of these samples at the time of the nuclear explosions are shown in Fig. 1.

The samples were crushed and pulverized to a grain size of $<74 \mu\text{m}$. From each powdered sample, a 20–30 g aliquot was packed in a plastic container of 54 mm i.d. and of depth 9 mm. γ -ray spectrometric measurements were made using heavily shielded coaxial type and/or planar type Ge(Li) detectors. To determine the counting efficiencies of the spectrometers as a function of photon energy, reference counting sources were also prepared by adding a known amount of ^{152}Eu standard solution to another 20–30 g aliquot of each powdered sample. Examples of the γ -ray spectra are shown in Fig. 2, in which neutron-induced radioactivities of ^{60}Co and ^{154}Eu were also identified along with natural radioactive nuclides. No such artificially-induced radioactivities were detected in γ -ray spectra of samples collected elsewhere in Japan. In the case where 30 g of powdered sample was measured for 4 days by the present counting method, the lower limit of the determination of ^{152}Eu in the sample was $\sim 0.67 \text{ Bq kg}^{-1}$ in concentration. The counting results for samples collected in Hiroshima and Nagasaki are given in Table 1 in units of Bq kg^{-1} indicating the concentration of neutron-induced radionuclide in the sample.

To determine the specific radioactivities of ^{152}Eu , ^{154}Eu and ^{60}Co , (the ratios of $^{152}\text{Eu}/\text{Eu}$, $^{154}\text{Eu}/\text{Eu}$ and $^{60}\text{Co}/\text{Co}$ in each sample) it was necessary to determine the concentration of the target elements Eu and Co in each sample. For this purpose, neutron activation analysis was carried out for a $\sim 100 \text{ mg}$ aliquot of each powdered sample, geochemical reference rock samples such as JB-1 (basalt, issued by the Geological Survey of Japan)², JG-1 (granodiorite, issued by the Geological Survey of Japan)² and W-1 (diabase, issued by the US Geological Survey)³ being used as reference standards. Neutron irradiation was carried out using TRIGA Mark II nuclear reactors at the Musashi Institute of Technology and at the St Paul's University (Rikkyo University). The concentrations of target elements in each sample thus determined are shown in Table 1. From these data, the specific radioactivities of ^{152}Eu , ^{154}Eu and ^{60}Co at the time immediately after the nuclear explosion were calculated, correcting for the radioactive decay that took place in the time between the nuclear explosion and our counting. In Fig. 3, the specific radioactivities of ^{152}Eu at the time immediately after the nuclear explosion are shown in relation to the slant distance from the explosion point of the nuclear weapon over Hiroshima and Nagasaki. Although it is difficult to know the exact energy spectrum of nuclear weapon neutrons irradiating the target elements in each sample, an apparent thermal neutron fluence, Φ (cm^{-2}), at each sample location can be estimated according to the equation:

$$\Phi = \frac{10^3 AA_r}{LX\sigma\lambda}$$

where, A is the specific radioactivity of the product (for example, ^{152}Eu) at the time immediately after the nuclear explosion (Bq mg^{-1}); A_r is the atomic weight of the target element (for example, Eu) (g mol^{-1}); L is the Avogadro con-

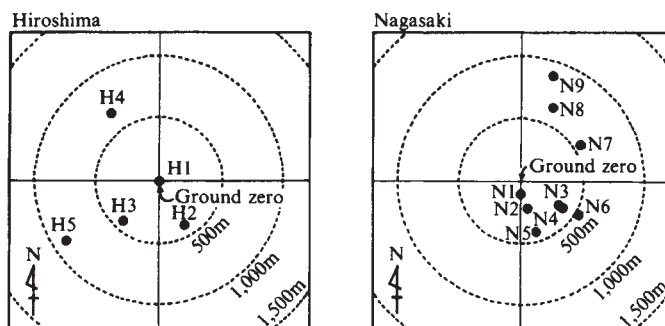


Fig. 1 Sampling locations. The concentric circles indicate ground distance from ground-zero. The explosion point, or air-zero point, of the nuclear weapon was $580 \pm 20 \text{ m}$ and $490 \pm 25 \text{ m}$ in the air over the ground-zero in Hiroshima and Nagasaki, respectively.

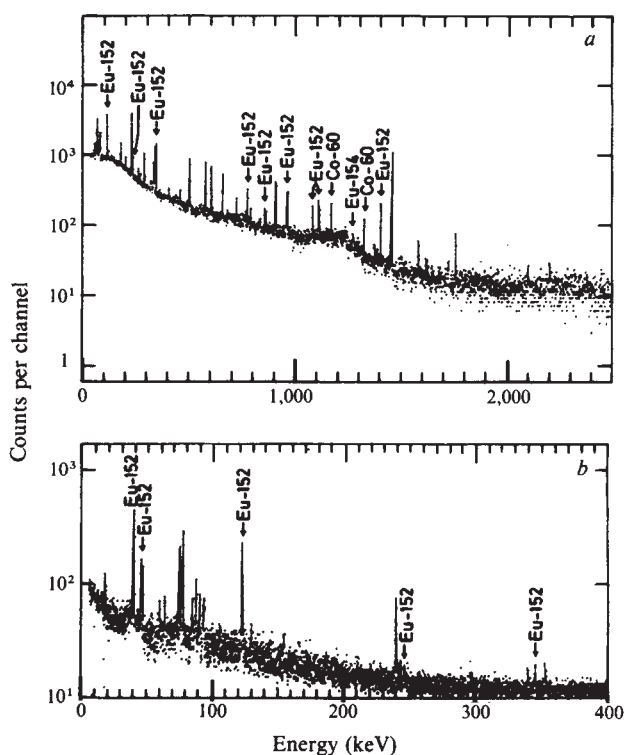


Fig. 2 γ -Ray spectra for 25.6 g of roof tile exposed to the nuclear explosion at ground-zero in Hiroshima (H1 in Fig. 1). Spectrum *a* was obtained by usual Ge(Li) coaxial detector (counting time 93.09 h) and *b* by low energy photon spectrometer in which planar type Ge(Li) detector was used (counting time 118.35 h).

stant (mol^{-1}); X is the natural isotopic abundance (atomic fraction basis) of the nuclide of interest in the target element, which in the case of ^{151}Eu in natural Eu is 0.479; σ is the thermal neutron cross-section (cm^2) for (n, γ) reaction of the target nuclide; and λ is the decay constant (s^{-1}) of the neutron-induced radionuclide such as ^{152}Eu . A few examples of the calculations are as follows: at the ground-zero in Hiroshima (H1 in Fig. 1 and Table 1), apparent thermal neutron fluences were estimated from $^{152}\text{Eu}/\text{Eu}$, $^{154}\text{Eu}/\text{Eu}$ and $^{60}\text{Co}/\text{Co}$ to be $(6.01 \pm 0.42) \times 10^{12} \text{ cm}^{-2}$, $(6.4 \pm 1.4) \times 10^{12} \text{ cm}^{-2}$ and $(7.9 \pm 0.8) \times 10^{12} \text{ cm}^{-2}$, respectively. The values of apparent thermal neutron fluence estimated in this work were compared with those estimated by Saito⁴ who was the first to determine residual neutron-induced radioactivity of ^{60}Co in iron materials collected in Hiroshima and Nagasaki. The values of thermal neutron fluence estimated by Saito on the basis of $^{60}\text{Co}/\text{Co}$ were: $2.39\text{--}2.75 \times 10^{12} \text{ cm}^{-2}$ at the Atomic Bomb Memorial Dome, Hiroshima ($\sim 600 \text{ m}$ from the explosion point), and $1.3\text{--}3.2 \times 10^{11} \text{ cm}^{-2}$ at the Nagasaki Medical College ($\sim 720 \text{ m}$ from the

Table 1 Neutron-induced radionuclides and target elements of (n, γ) reaction in samples exposed to the nuclear explosion in Hiroshima and Nagasaki

City	Sample location and type	Slant distance from the explosion point (m)	Time interval between explosion and counting (yr)	Concentration of radionuclide in sample (Bq kg^{-1})*	Concentration of target element in sample (mg kg^{-1})
Hiroshima	H1, roof tile	580 $\pm$ 20	32.107	^{152}Eu : 28.2 $\pm$ 0.7	Eu: 1.38 $\pm$ 0.07
	H1, roof tile	580 $\pm$ 20	32.107	^{154}Eu : 1.32 $\pm$ 0.26	Eu: 1.38 $\pm$ 0.07
	H1, roof tile	580 $\pm$ 20	32.107	^{60}Co : 4.22 $\pm$ 0.33	Co: 23.0 $\pm$ 0.2
	H2, roof tile	710 $\pm$ 30	32.578	^{152}Eu : 5.32 $\pm$ 0.50	Eu: 1.33 $\pm$ 0.04
	H3, roof tile	720 $\pm$ 30	32.553	^{152}Eu : 9.09 $\pm$ 0.65	Eu: 1.88 $\pm$ 0.06
	H4, roof tile	890 $\pm$ 80	32.562	^{152}Eu : 1.15 $\pm$ 0.54	Eu: 1.42 $\pm$ 0.04
	H5, roof tile	1,050 $\pm$ 40	32.570	^{152}Eu : 0.84 $\pm$ 0.26	Eu: 1.32 $\pm$ 0.03
Nagasaki	N1, roof tile	500 $\pm$ 40	32.499	^{152}Eu : 11.25 $\pm$ 0.91	Eu: 0.82 $\pm$ 0.03
	N2, roof tile	540 $\pm$ 30	32.060	^{152}Eu : 10.49 $\pm$ 0.44	Eu: 1.44 $\pm$ 0.07
	N3, roof tile	610 $\pm$ 30	32.395	^{152}Eu : 19.70 $\pm$ 0.48	Eu: 1.59 $\pm$ 0.03
	N3, rock	610 $\pm$ 30	31.841	^{152}Eu : 2.61 $\pm$ 0.22	Eu: 0.97 $\pm$ 0.02
	N4, rock	620 $\pm$ 30	32.370	^{152}Eu : 1.77 $\pm$ 0.23	Eu: 1.20 $\pm$ 0.02
	N5, roof tile	650 $\pm$ 40	32.510	^{152}Eu : 4.91 $\pm$ 0.86	Eu: 1.68 $\pm$ 0.05
	N6, rock	720 $\pm$ 30	32.447	^{152}Eu : 0.72 $\pm$ 0.18	Eu: 1.03 $\pm$ 0.01
	N6, rock	720 $\pm$ 30	32.348	^{152}Eu : 1.90 $\pm$ 0.31	Eu: 1.03 $\pm$ 0.01
	N7, rock	740 $\pm$ 40	32.381	^{152}Eu : 0.68 $\pm$ 0.20	Eu: 0.95 $\pm$ 0.02
	N7, brick	740 $\pm$ 40	32.466	^{152}Eu : 1.22 $\pm$ 0.28	Eu: 0.81 $\pm$ 0.01
	N8, roof tile	810 $\pm$ 30	32.518	^{152}Eu : 0.95 $\pm$ 0.24	Eu: 1.73 $\pm$ 0.05
	N9, rock	1,000 $\pm$ 30	32.532	^{152}Eu : 0.81 $\pm$ 0.20	Eu: 0.92 $\pm$ 0.01

* Concentration at the time of the counting in this work.

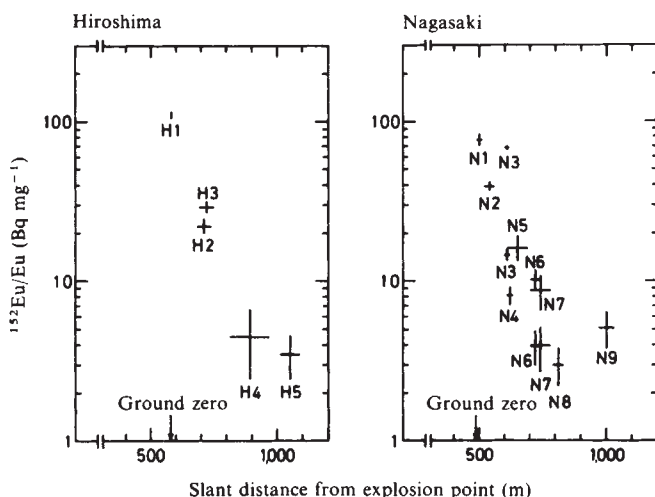


Fig. 3 Specific radioactivity of ^{152}Eu immediately after the nuclear explosion.

explosion point). The values estimated in this work on the basis of $^{152}\text{Eu}/\text{Eu}$ were: $2.5\text{--}8 \times 10^{12} \text{ cm}^{-2}$ (interpolated) at the Atomic Bomb Memorial Dome, Hiroshima, and $1.0\text{--}3.3 \times 10^{11} \text{ cm}^{-2}$ at the Nagasaki Medical College. Our estimates of apparent thermal neutron fluence therefore do not differ much from those of Saito. Although, after the work of Saito, Hashizume *et al.*^{5,6} determined specific radioactivity of ^{60}Co in iron materials collected from an appropriate depth in concrete walls which were exposed to the nuclear explosion in Hiroshima or Nagasaki, they reported only the dose to the air due to fast neutrons at various locations. Our ^{152}Eu data show the decreasing tendency of apparent thermal neutron fluence with increasing slant distance from the explosion point in both cities, although rather scattered values were observed in Nagasaki owing to its complex geographical features.

The radionuclides such as ^{152}Eu which remain in samples exposed to the 1945 nuclear explosions are of importance for the re-evaluation of neutron dose from the explosions especially as the problem is now under discussion in the United States⁷ and Japan from the viewpoint of biological effects of ionizing radiations. For more sensitive measurements, chemical separation to enrich europium and cobalt will be effective, and the depth profile of the neutron induced ^{152}Eu activity in thick

sample may provide information on the energy spectrum of nuclear weapon neutrons irradiating the surface of the sample.

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Crustal thinning and subsidence in the North Sea

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We present here the results of a detailed study of subsidence and crustal thinning across the Central Graben of the North Sea basin. Two independent lines of evidence have been used to test how well the uniform extensional model^{1,2} can account for the evolution of the North Sea basin. A long range seismic profile was shot perpendicular to the Central Graben from Edinburgh to southern Norway and data were analysed from 11 exploration wells situated close to the seismic line (Fig. 1). The estimates of β , the increase in surface area due to extension, from the crustal structure determined using the seismic data and from the well subsidence patterns are both compatible with a simple uniform extensional mechanism for the post-Palaeozoic evolution of the North Sea.

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The seismic refraction data were collected with a sea-bottom array of 12 Pull-Up Shallow-water Seismometers (PUSSs) in the Central Graben. Shots were fired from the RRS *John Murray* at ranges of 0–300 km either side of the array (Fig. 1). A composite record section of seismograms from all receivers indicated that the arrivals would not fit a plane layered or

laterally homogeneous model. A set of time terms to the Moho was obtained for the experimental section, and converted to depth to give an initial structure for forward modelling. The crustal model was refined using Cassell's program³, Raysyn, for the calculation of synthetic seismograms in laterally varying media. Zechstein to Recent deposits were included in the model in simplified form using sediment thickness⁴ and velocity data (P. A. Ziegler, personal communication) (Fig. 2b). The remainder of the crust down to the Moho was modelled with seismic velocities which varied continuously both horizontally and vertically. Synthetic seismograms generated by Raysyn from this model satisfy the travel-time and amplitude characteristics of the records from each shot into the array. The seismic model was further constrained by modelling the gravity field. The seismic velocity structure was converted to densities using the Nafe–Drake velocity–density curves⁵ and a two-dimensional gravity profile was then calculated. This procedure gave a lithospheric density structure in isostatic equilibrium and a gravity profile which matches the observed field to within about 5 mgal. The resulting model has the Moho at a depth of 20 km beneath the Central Graben (Fig. 2c). A Moho depth of 20 km beneath the Central Graben was previously predicted from models derived from gravity data by Donato and Tully⁶. The east–west asymmetry in both the crustal thickness and velocity distribution suggests that lateral variations exist in the pre-Permian basement.

Basement subsidence paths have been calculated for 11 wells close to the seismic profile. The effect of sediment compaction

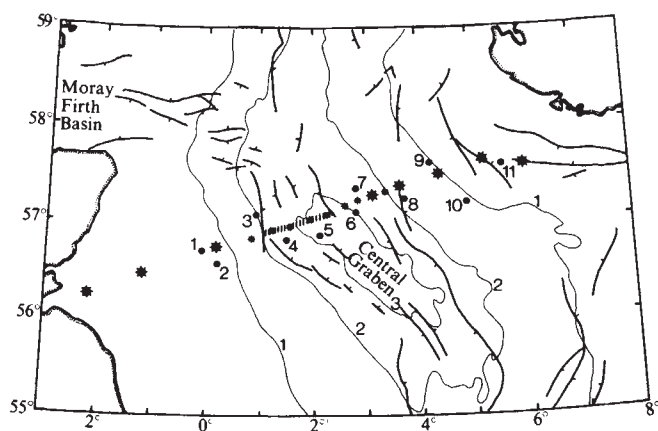


Fig. 1 Location map. Heavy lines, major faults; fine lines, Tertiary sediment isopachs in km; slashed line, PUSS array; stars, shot points with shots <500 kg indicated by the small stars, Numbered circles, well positions.

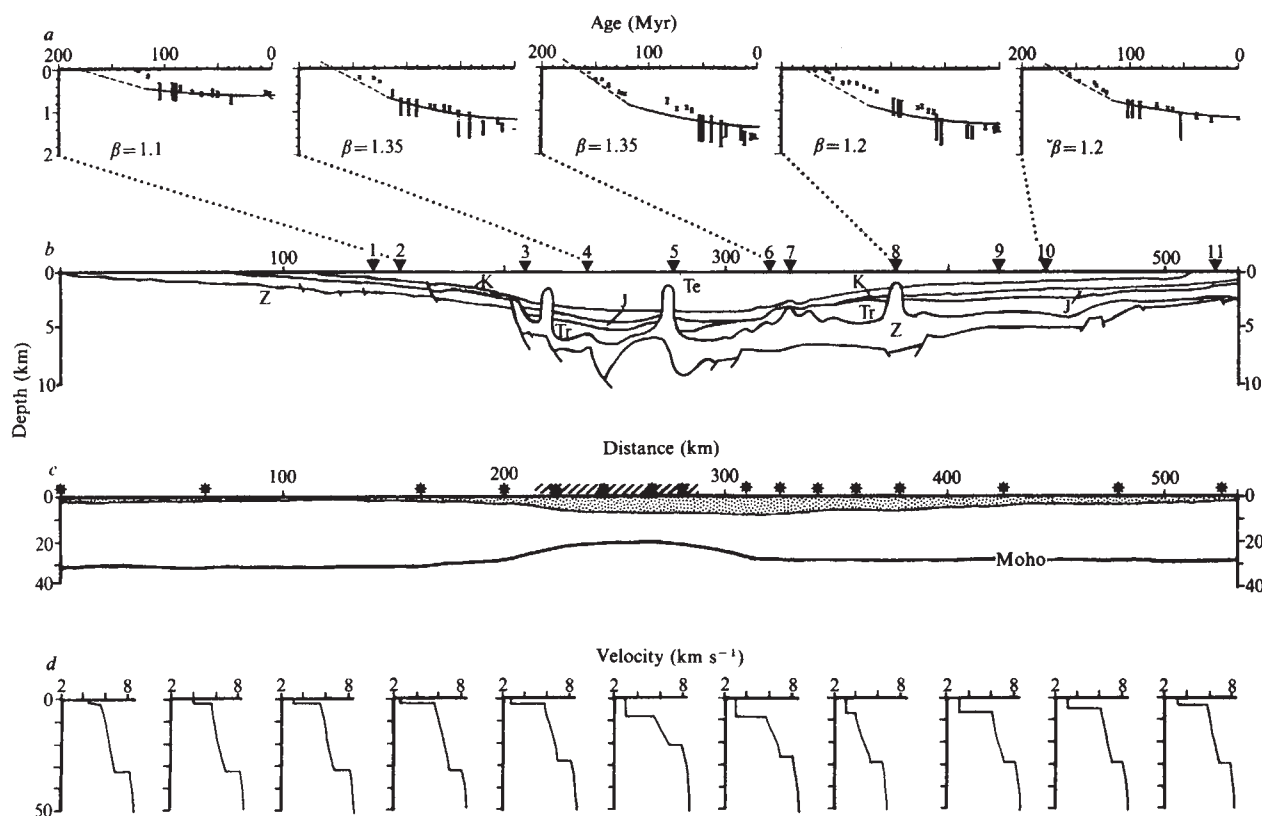


Fig. 2 Subsidence and structural data across the Central Graben. *a*, Subsidence paths for five of the wells after removing the effect of sediment compaction and loading. Hence the present day unloaded basement level is at a shallower depth than observed in the geological section below. Bars, range of basement level; dashed line, predicted fault-controlled subsidence; heavy line, predicted thermal subsidence; β , estimate of crustal thinning. The theoretical curves were calculated using the pre-Jurassic crustal thicknesses shown in Table 1. The mismatch in the initial subsidence is shown by the projection of the dashed line above zero depth. *b*, Geological section along the seismic profile after Ziegler (personal communication) and Day *et al.*⁶. Te, Tertiary; K, Upper Cretaceous; J, Lower Cretaceous and Jurassic; Tr, Triassic; Z, Zechstein. Arrows indicate well position projected onto the line of section. Vertically exaggerated five times. *c*, Seismic crustal model; Stippled area, Zechstein to Recent sediments; heavy line, position of the Moho constrained to within 1 km; stars, shot points; slashed line, PUSS array. No vertical exaggeration. *d*, Velocity–depth profiles at 50-km intervals along the seismic section, showing variation in crustal character with distance.

Table 1 Comparison of estimates of extension from the seismic profile and from the well subsidence across the Central Graben

Wells	1	2	3	4	5	6	7	8	9	10	11
Present crustal thickness from the seismic model (km)	31	31	24	18	17	25	26	26	26	27	28
β from the seismic model assuming an initial crustal thickness of 31 km	1	1	1.3	1.7	1.8	1.25	1.2	1.2	1.2	1.2	1.2
Mismatch between observed and predicted initial subsidence, assuming an initial crustal thickness of 31 km (m)	—	—	550	750	650	350	400	—	—	100	150
Mismatch between observed and predicted initial subsidence, using crustal thicknesses shown below (m)	—	—	50	100	100	150	150	—	—	100	150
Pre-Jurassic crustal thickness assumed for best fit β s shown below	31	31	28	25	25	28	28	31	31	31	31
β estimated from well data	1.1	1.1	1.2	1.35	1.55	1.35	1.2	1.2	1.2	1.2	1.2

and loading, and palaeo-water depth, were accounted for during backstripping, to give the subsidence history of the basin when filled with water only, thus enabling direct comparison with theoretical subsidence curves. The wells were subdivided using a biostratigraphy based on the occurrence of foraminifera⁷, and using a lithostratigraphy based on geophysical log characteristics⁸. All Triassic and older deposits were assumed to have been completely compacted before the Middle Jurassic extension event. All younger units were decompacted using the method described by Sclater and Christie⁹, allowing the sedimentary section to be reconstructed to its original thickness at each time interval. The depth of water during the deposition of the sediments was estimated by comparing assemblages of fossil foraminifera separated from the drill cuttings, with assemblages found in known environments in the present day oceans. Where foraminiferal evidence was sparse geological and palaeogeographical evidence¹⁰ has been used to help determine the palaeobathymetry. Eustatic changes in sea level should be taken into account to relate the level of the basement to present day sea level. However, because of the problems in determining the amplitude of these changes we assumed that there have not been any eustatic variations in sea level. Comparisons of synthetic gravity anomalies across the basin with the gravity field obtained from Seasat altimetry data (D. Lelgemann, personal communication) showed that the lithosphere beneath the North Sea has negligible elastic thickness. The wells were therefore backstripped assuming that the load was locally compensated. Because of the uncertainties in the water depth determinations there is a range of possible basement values constrained by the maximum and minimum water depth for that time (Fig. 2a).

The main faulting event which produced the present configuration of the North Sea lasted ~60 Myr and started in the Middle Jurassic. This period of rifting was followed by a general steady subsidence resulting in the present saucer-shaped basin. The well subsidence was therefore modelled assuming steady extension² over 60 Myr with an initial crustal thickness of 31 km and crustal density of 2.8 g cm⁻³. The theoretical curve was chosen to give the closest fit to the thermal part of the subsidence, while not exceeding the amount of initial subsidence apparent in the well. There was good agreement between observations and predictions for the marginal wells (Figs 1, 2b; wells 1, 2, 8–11). However, for the central wells the initial subsidence predicted by the model exceeded that observed by >300 m (Table 1). When estimates of the extension factor, β from the wells were compared with those obtained from the seismic crustal model a similar pattern emerged. While there was good agreement between the two estimates on the margins, estimates from the central wells gave values of β from the subsidence which were lower than those from the seismic model. This disagreement is not surprising since the seismic model gives the integrated effect of all crustal events, whereas the well study provides information concerning the post-Middle Jurassic events. Hence the difference between the estimates of β sug-

gests that there was an earlier stretching event in the Graben. Therefore the theoretical curves were recalculated for the central wells using smaller values for the initial crustal thickness, with the assumption that the thermal effects of any earlier stretching event had decayed by Middle Jurassic times. The agreement between the predicted and observed subsidence for wells 3–7 was improved (Table 1). The postulated earlier stretching event is compatible with the geological evidence for the initiation of the major graben system during the Triassic¹⁰.

The post Mid-Jurassic stretching factors estimated from the well data (Table 1) are slightly lower than those suggested by earlier subsidence studies⁹ in the Central Graben (maximum $\beta = 1.5$ –2.0), which did not take account of water depth at the time of sediment deposition and assumed instantaneous stretching during Albian/Aptian times. Estimates of the stretching factor based on measurements of extension of basement faults seen in multichannel reflection data¹⁰ have so far been consistently lower than estimates from well subsidence or crustal profiles; however, the amount of overall extension represented by the configuration of a fault is a controversial subject^{11,12}.

The results presented here from the seismic refraction experiment and the subsidence history show that a uniform extensional model can account for the major features of the post-Palaeozoic evolution of the North Sea. If the initial crustal thickness was 31 km, the seismic model indicates an extension in the plane of the section of about 110 km ($\beta = 1.25$) across the Central Graben, but provides no information about when this extension occurred. The subsidence patterns indicate that 50–80 km of the extension happened during the Middle Jurassic to Early Cretaceous rifting event.

A more detailed paper is in preparation that will describe the methods, analyses and interpretation of the two lengthy studies summarized here.

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Amino acid analysis of Pleistocene marine molluscs from the Gower Peninsula

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The Gower Peninsula, South Wales is a particularly important area, where marine, terrestrial, glacial and non-glacial sediments occur in stratigraphical sequence¹. The establishment of a Pleistocene aminostratigraphy where stratigraphical relationships are well established would make it possible to include Pleistocene deposits elsewhere in this stratotypic framework thereby expanding it. Sampling of sites in Devon, Cornwall, Dorset and Sussex is now being carried out to extend aminostratigraphical correlation of the Pleistocene beaches of southern Britain. Extensive sampling of the Pleistocene beaches of the Gower Peninsula, was carried out during 1981 when specimens of *Patella vulgata* (Linnaeus) and *Nucella lapillus* (Linnaeus) were collected for amino acid analysis (Fig. 1). Amino acid analysis is fundamental to the identification of mixed-age populations which, it has been discovered, are common in most beach deposits. This is particularly important because successive high sea-level stands have probably occupied the coast on several occasions, leaving only one extensively reworked deposit as evidence for several marine incursions. If a molluscan fauna was associated with each high stand of sea-level and has been preserved in part, the multiple occupation of these sites can be confirmed and their relative ages resolved.

The most common beach facies is a poorly sorted high-energy deposit containing pebbles and cobbles of local and other rocks². The subangular to rounded clasts (dependent on rock type) are contained in a matrix of medium grained sand and comminuted shell debris. The larger clasts commonly form a framework infilled with finer grained sediment, for example, at Shirecombe (GR SS 543 875, Fig. 1). More rarely, the larger clasts are suspended in the finer grained matrix, for example, at Hunts Bay West (GR SS 562 868, Fig. 1). It is suggested that this facies, lithofacies A, represents a high-energy beach deposit which accumulated near high tide mark and may be in part storm-generated.

There are two exceptions to the lithofacies described above. The first is the inner beach unit¹ at Minchin Hole Cave (GR SS 555 868, Fig. 1) which represents an intertidal beach facies deposited in moderate energy conditions. Specimens of *P. vulgata*, *N. lapillus* and *Littorina* species occur in a medium grained sand deposit with shingle layers. This facies, termed lithofacies B, is stratigraphically older than an outer beach¹ of storm-derived deposits (lithofacies A) which T.N. George called the *Patella* beach².

The Pleistocene beach at Horton (GR SS 483 855, Fig. 1) differs from both facies described above. It consists of subangular to rounded clasts in a red fine sand-clay matrix¹⁰ (lithofacies C). The clasts include local rock types and erratics. *N. lapillus*, *Littorina littorea* (L.) and *Littorina littoralis* (L.) are particularly abundant and *P. vulgata* has also been recorded¹. Lithofacies A also occurs here but is only preserved in gullies at a slightly lower elevation than lithofacies C. The relationship between the two beaches is not clear because they outcrop approximately 5 m apart.

All of the fauna found in lithofacies A, B and C have been transported to some degree as indicated by the fracturing and abrasion of the shells. No fauna have yet been found *in situ*, for example, articulated bivalves and shells in life position. The shell assemblages are all thanatocoenoses. Most preserved shells are adult forms, the younger population having been

winnowed out during sedimentation. All of the lithofacies have only the mechanically strongest shells preserved, confirming that deposition of all three lithofacies occurred in moderate to high-energy, agitated water conditions.

The clay content of lithofacies C is an enigma. The relatively high clay content of this deposit suggests lower energy conditions of sedimentation, but the high proportion of rounded pebbles and fractured and abraded shells are compatible with high-energy conditions of deposition. It is proposed that this facies was sedimented in high-energy conditions and has subsequently been reworked and mixed with the sediments of the drift terrace in that area by subaerial processes. No evidence of a younger marine fauna has been found in this deposit which precludes reworking by marine processes.

Samples were analysed at INSTAAR Amino Acid Laboratory, University of Colorado, and at the Aberystwyth Amino Acid Geochronology Laboratory. The methods of shell preparation and amino acid analysis are fully described in refs 3, 4. A standard mixture of amino acids was run regularly during analysis at both laboratories to ensure that the analysers were producing consistent results. An internal standard, norleucine, is also used and is added during the preparation stage.

The quantities of the amino acids are recorded by a computing integrator and on a dual pen strip-chart recorder. The amino acids are then identified by their retention time. The amino acid analysers are adjusted to give the maximum resolution of D-alloisoleucine and its diastereomer L-isoleucine, however, aspartic acid to tyrosine are all well resolved.

The D-alloisoleucine to L-isoleucine ratio is used as a relative index of age because these isomers can easily be separated by HP ion-exchange liquid chromatography. L-isoleucine epimerizes to D-alloisoleucine on death of the mollusc. The D-alloisoleucine to L-isoleucine ratio increases from 0 in a recently dead specimen to an equilibrium ratio of 1.3 ± 0.05 (ref. 3). The length of time needed to reach equilibrium is dependent on species and temperature³. To circumvent thermal variation, samples have been analysed from a limited geographical region, over which the temperature fluctuations, while unknown, can be assumed to have affected the region uniformly³. In such a

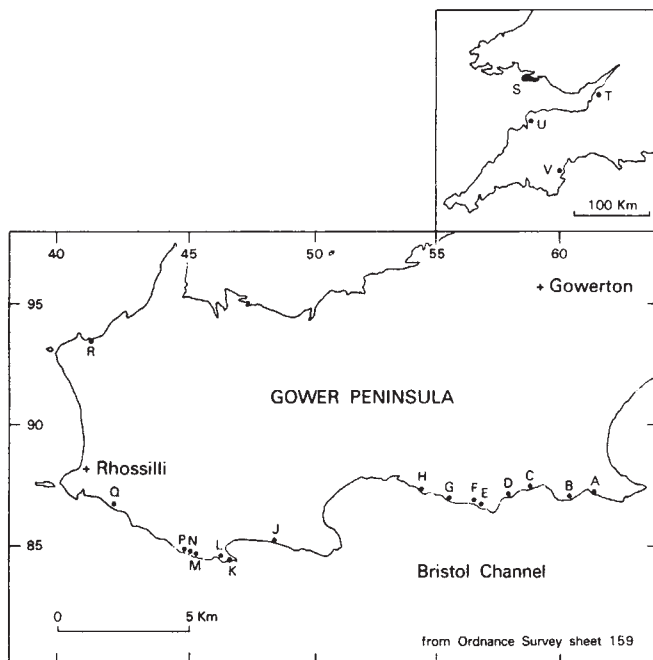


Fig. 1 Location of sample points on the Gower Peninsula, South Wales: A, Rothers Sker; B, Snaple Point; C, Brandy Cove; D, East of Pwll Du; E, Hunts Bay East; F, Hunts Bay West; G, Minchin Hole Cave; H, Shirecombe; J, Horton; K, East of Culver Hole; L, Overton; M, Site 25; N, Site 26; P, Site 27; Q, Mewslade West; R, Broughton; S, Gower Peninsula; T, Swallowcliff; U, Saunton; V, Torquay.

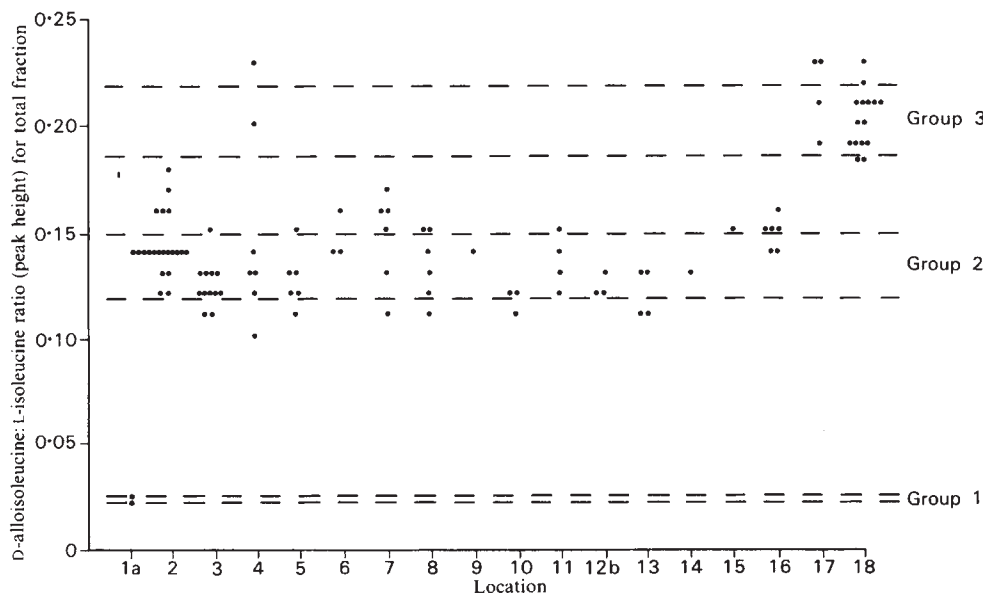


Fig. 2 D-alloisoleucine: L-isoleucine ratios for *Patella vulgata*.

region, amino acid ratios may be used directly as correlation and relative age indices³.

Shells were taken from the surface of the deposits and from varying depths and showed a <2% variation in their amino acid ratios. For a particular species, the same parts of each shell were selected for analysis. In the case of *P. vulgata*, the outer margin of the shell was sampled. For *N. lapillus*, the outer lip of the body whorl was sampled. Analyses of the different parts of the shells were carried out on several species. Minimal differences in the D-alloisoleucine to L-isoleucine ratio were found between the apex, mid-shell/columella and outer margin/outer lip of the body whorl of *P. vulgata* and *N. lapillus* respectively.

All data below refer to the D-alloisoleucine to L-isoleucine ratio of the total (free + bound) amino acid fraction, in terms of peak height measurements. Three groups are apparent in the data of *P. vulgata* (Fig. 2). Group 1 has a mean ratio of 0.0255 ± 0.0015 ($n = 2$) and this represents control samples from the modern beaches of the Gower Peninsula. Group 2 has a mean ratio of 0.134 ± 0.016 ($n = 83$). Group 3 is based on samples from Saunton, Devon; Hopes Nose, Torquay, Devon; Swallowcliff, Avon and the inner beach (lithofacies B), Minchin Hole Cave, Gower, which gave a mean value of 0.203 ± 0.016 ($n = 20$). Older elements have been observed in the results of *P. vulgata* from lithofacies A (which mostly gave results falling in group 2) at Minchin Hole outer beach (GR SS 555 868, Fig. 1), Hunts Bay East (G.R. SS 566 865, Fig. 1) and Gower site 25 (GR SS 452 849, Fig. 1). As sample contamination during collection, preparation and analysis was not encountered these samples probably represent shells reworked from older deposits. *P. vulgata* data from Minchin Hole inner beach (GR SS 555 868, Fig. 1) samples fall into group 3 (Fig. 2), confirming that the inner beach unit is older than the outer beach, and thereby adding aminostratigraphical amplification to the already established lithostratigraphical demonstration of two separate beaches¹. Earlier analyses of Minchin Hole samples⁵ from the outer beach produced seemingly lower ratios but it has been demonstrated that these differences (between the 1977–79 and 1981 data) are because of the variance in sample preparation procedures⁶. The data from INSTAAR and from the Aberystwyth Amino Acid Geochronology Laboratory are closely comparable. Nine shells of *P. vulgata* from lithofacies A at Minchin Hole Cave were analysed at INSTAAR and gave a mean of 0.14 ± 0.015 . Fragments of the same nine shells gave a mean of 0.139 ± 0.0009 on the Aberystwyth analyser.

The data of *N. lapillus* (Fig. 3), exhibit two groups of ratios. Group 1 (Fig. 3) has a mean value of 0.138 ± 0.015

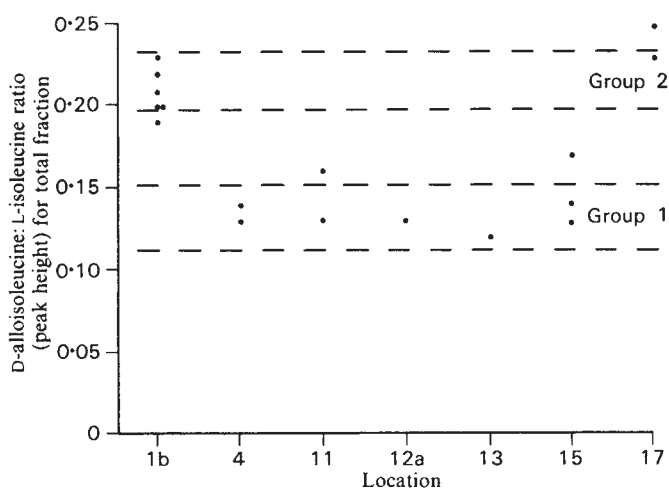


Fig. 3 D-alloisoleucine: L-isoleucine ratios for *Nucella lapillus*. Locations (lithofacies)—1a Horton (modern); 1b Horton (C); 2 Minchin Hole (A); 3 Snaple Point (A); 4 Hunts Bay east (A); 5 Hunts Bay west (A); 6 E. of Culver Hole (A); 7 Site 25 (A); 8 Site 26 (A); 9 Site 27 (A); 10 Mewslade West (A); 11 Rothers Sker (A); 12a E. of Brandy Cove (A); 12b Brandy Cove (A); 13 E. of Pwll Du (A); 14 Overton (A); 15 Broughton (A); 16 Shirecombe (A); 17 Minchin Hole (B); 18 Older group based on Saunton, Hopes Nose and Swallowcliff.

($n = 9$) and group 2 has a mean value of 0.216 ± 0.018 ($n = 8$). The lower values, group 1, represent samples from lithofacies A and the higher values, group 2, represent samples from lithofacies C at Horton (GR SS 483 855, Fig. 1) and from lithofacies B at Minchin Hole inner beach (GR SS 555 868, Fig. 1).

The data presented (Figs 2, 3) constitute a relative age framework for the marine Pleistocene deposits of Wales. Any estimation of age must arise through studies of the isoleucine epimerization kinetics of *P. vulgata*—as this is the most commonly occurring species—or through a reliable uranium-series date on carbonate material from these beach deposits. The exact temperature history of the deposits on the Gower Peninsula is not known, therefore one must be cautious if using these data to estimate the geochronometric age of the deposits.

A uranium-series date of ~121 kyr BP was obtained from the travertine cement of the 8-m raised beach in Belle Hougue Cave, Jersey⁷. This is the only available uranium-series date

from a British site where amino acid analyses have been carried out on shell material⁷. The mean amino acid ratio (D-alloisoleucine to L-isoleucine) for *P. vulgata* at Belle Hougue Cave is 0.123 ± 0.02 (ref. 7) and this is comparable to group 2 of the data presented here (Fig. 2).

The latitudinal and consequential temperature differences between Jersey and Gower would affect the rate of isoleucine epimerization in the shells and the resulting amino acid ratios³. An estimate of the age of the Gower deposits may be made assuming that this effect is not significant. On this basis, an amino acid ratio for *P. vulgata* of 0.123 would represent an age of ~121 kyr BP. Using this absolute age to determine the rate constant of the kinetic equation⁸ for *P. vulgata*, an estimation of the geochronometric age of a deposit may be made even though the activation energy (E_a) of the species remains unknown. On this basis, the *P. vulgata* of group 2 would give an age of ~134 kyr BP and group 3 would give an age of ~208 kyr BP. This would support a correlation of group 2 *P. vulgata* ratios with deposits of oxygen isotope stage 5e age (125 kyr BP)⁹ and group 3 ratios would be likely to represent deposits of oxygen isotope stage 7 age (210 kyr BP)⁹. The isoleucine epimerization kinetics of each molluscan species are different and direct comparison of amino acid ratios between species cannot be made. However, the isoleucine epimerization kinetics of *P. vulgata* and *N. lapillus* appear to be similar as the two species from the same sites give comparable ratios, therefore cautious intercomparison is permissible. On this basis, the group 1 *N. lapillus* ratios might represent an age of ~137 kyr BP and the group 2 ratios might represent an age of ~221 kyr BP. Therefore group 1 of the *N. lapillus* data (Fig. 3) probably represents stage 5e (125 kyr BP)⁹ and group 2 probably represents stage 7 (210 kyr BP)⁹.

Most of the deposits on the Gower Peninsula are likely to be of stage 5e age (125 kyr BP) although certain of the deposits contain an older faunal element which may represent reworking of stage 7 (210 kyr BP) sediment. The only remaining evidence of this deposit is the inner beach (lithofacies B) at Minchin Hole Cave (Fig. 1) and lithofacies C at Horton (Fig. 1). Other such deposits in the area either remain unexposed or have been totally eroded.

The Pleistocene beach deposits of Hopes Nose, Torquay, Devon; Saunton, Devon; Swallowcliff, Avon and Minchin Hole inner beach (lithofacies B) (Fig. 1) are probably of oxygen isotope stage 7 (210 kyr BP)⁹ age.

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Note that analysis numbers are as follows—INSTAAR, Amino Acid Geochronology Laboratory: AAL 2227-40, 2276-77, 2279, 2283-85, 2288-95, 2297, 2300, 2364, 2366, 2370 and 2372-74; Aberystwyth Amino Acid Geochronology Laboratory: ABER 26 and 28-36.

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Selective dissolution of siliceous microfossils observed in a box core from the north-east equatorial Pacific

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A box core taken at 11°50.3' N and 137°28.2' W in the Central Pacific manganese nodule province was studied to determine the pattern of diatom and radiolarian preservation with depth in the sediment, as well as to observe downcore variations in clay mineralogy. We observed marked deterioration of the siliceous microfossils within the upper 30 cm of this sediment; over this depth interval the Quaternary diatoms disappear first, followed deeper downcore by the dissolution of Quaternary radiolarians. Tertiary microfossils in general were the most corrosion resistant, and the residual microfossil assemblage in the lower part of the core consisted of fragmented, robust Tertiary forms. Consequently, the apparent biostratigraphical age of the sediment appeared much greater than the age suggested by mineralogical and radioisotopic data.

In an area north-east of our site, at 14° N and 117° W, Johnson¹ found that siliceous microfossil preservation was excellent in the surface sediments but deteriorated markedly 1-2 m below the sea floor, where biogenic opal was totally absent. Coincident with this disappearance of biogenic opal, there was an increase in the percentage of smectite relative to the other clay minerals. It was suggested that the silica released by postburial dissolution may have been involved in the formation of authigenic smectite. The sedimentation rate at Johnson's site was ~0.4 cm kyr⁻¹, whereas the core used in this work taken from DOMES Site B, station 55 (water depth 4,982 m) indicated a much smaller sedimentation rate of 0.04 cm kyr⁻¹ based on ²³⁰Th excess dating². As a consequence of the greater time available to the surface sediments here, marked deterioration of the siliceous microfossils was observed at a much shallower depth in this sediment, that is, within 30 cm of the sea floor. It was also observed that over this short interval, selective dissolution first removed the diatoms, and deeper downcore, the radiolarians were dissolved. The clay assemblage showed no change, however, over the length of the core.

The diatoms were analysed by observing strewn slides of the sediment samples with a light microscope under ×500 magnification. Separate sediment aliquots were sieved through a 63-μm mesh to extract the radiolarians. The radiolarians were washed off the sieve, taken up by an eyedropper, then placed on a slide and observed under ×250 magnification. The clay mineralogy was determined by X-ray diffraction. Details of the procedure may be found in ref. 3.

The results of this study are shown in Table 1 and Fig. 1. In the uppermost 11 cm of this core, there are well preserved Quaternary diatoms and radiolarians of age <500,000 yr BP. Less than ~3% reworked Tertiary radiolarians and only rare Tertiary diatoms were observed. Also, the number of individual tests is high in this zone. There were approximately 74,500 radiolarians and 1,600,000 diatoms per gramme of dry sediment taken from the 6-7 cm interval.

Below 11 cm, there is an abrupt decline in the Quaternary diatoms leading to a dominance of corroded and fragmented robust mid-Miocene forms. At the 17-18-cm interval, the number of diatoms per gramme decrease by an order of magnitude to 150,000 individuals. The radiolarians on the other hand, do not show evidence of corrosion until deeper in the core, at

Table 1 Siliceous microfauna observed in DOMES Site B core

Depth (cm)	Quaternary radiolarians									Miocene radiolarians		% Radiolarian fragments	Quaternary diatoms			Miocene diatoms	
	<i>Amphirhopalum ypsilon</i>	<i>Lithopera bacca</i>	<i>Theocorythium trachelium</i>	<i>Anthocyrtidium angulare</i>	<i>Theocorythium vetulum</i>	<i>Pterocanium praetextum</i>	<i>Lamprocyclas maritima</i>	<i>Ommatartus tetrathalamus</i>	<i>Spongaster tetras</i>	<i>Dorcadospirys dentata</i>	<i>Lynchocanoma elongata</i>		<i>Pseudoeunotia doliolus</i>	<i>Thalassiosira oestrupii</i>	<i>Nitzschia marina</i>	* <i>Cascinafiscus nodulifer</i>	<i>Actinocyclus ingens</i>
3-4	—	—	F	F	F	R	R	F	R	—	—	5-10	F	C	F	F	R
5-6	R	—	F	R	F	R	—	F	R	—	R	10-20	F	C	R	F	R
10-11	—	—	F	R	R	—	R	F	—	—	—	10-15	F	C	R	F	R
11-12	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	R	F	R	F	R
12-13	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	R	R	R	R	R
15-16	—	—	F	F	R	—	R	R	—	—	R	45-50	R	R	R	R	R
17-18	R	R	R	R	R	—	R	R	R	R	—	20-25	R	R	R	—	R
+20-21	—	—	R	R	—	—	R	—	—	F	—	50-60	R	—	R	R	R
+20-21	—	—	R	—	—	—	R	—	—	F	—	45-50	—	—	—	R	R
24-26	—	—	—	—	—	—	—	—	—	R	—	80-90	—	—	—	—	—
28-30	—	—	—	—	—	—	—	—	—	F	—	80-90	—	—	—	—	R

—, Absent; R, rare; F, few; C, common; +, separate aliquots of sample; NA, not analysed.

* Ranges from mid-Miocene to Recent.

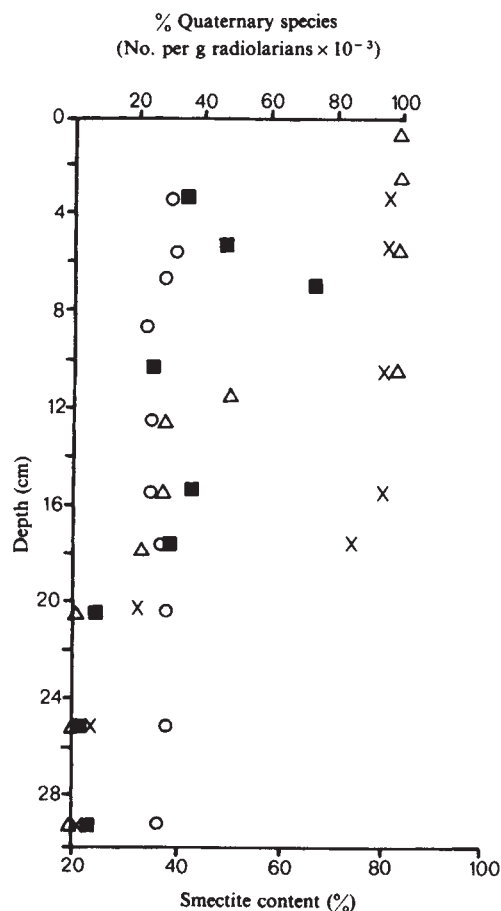


Fig. 1 The percentage of smectite (○) [of the clay fraction] and percentage of Quaternary radiolarians (X) and diatoms (Δ) [of their respective total assemblage] plotted against depth downcore for Domes Site B, station 55. Also shown is the downcore decrease in the total number of radiolarians per gramme of sediment (■).

20-21 cm, where the number of radiolarians begins to decrease sharply and a residual, robust Tertiary assemblage appears.

Several investigators^{1,4} have shown that in approximately the upper 30 cm of slowly accumulating siliceous clay sediments the pore waters are undersaturated with respect to SiO₂. It is not surprising then that intense dissolution of especially the more fragile siliceous tests would occur over that depth range. Furthermore, in laboratory experiments, Mikkelsen⁵ ascertained an order of selective dissolution for siliceous tests whereby radiolarians are most resistant to corrosion, diatoms are considerably less resistant, and silicoflagellates are the least resistant. She also found that the fragmentation of the residual diatom valves increased with time. Several investigators⁶⁻⁸ have also noted that the wall thickness of Tertiary species is greater than that of Quaternary species, and thus Tertiary microfossils are more corrosion resistant than those of the Quaternary. These observations probably explain the pattern of microfossil abundance seen downcore here: (1) there are abundant Quaternary diatoms and radiolarians in the bioturbated layer of the sediment; (2) below this the more fragile Quaternary diatoms disappear leaving a residual fragmented, more robust Tertiary diatom assemblage and the Quaternary radiolarian assemblage; (3) further downcore Quaternary radiolarians disappear leaving a residual, fragmented robust Tertiary assemblage.

This preservation sequence suggests that the Tertiary biostratigraphy observed at depth in the core, which is indicated by the presence of solely Tertiary forms, results from dissolution and does not reflect the true sediment age. The sedimentation rate derived from excess ²³⁰Th dating² is quite low (0.04 cm kyr⁻¹) and indicates that the bottom of the core was deposited ~750,000 yr ago. This is still much younger than the apparent biostratigraphical age.

Deep-sea sediments deposited beneath the calcium carbonate compensation depth (4,500-5,000 m in the tropical Pacific) are devoid of coccoliths and planktonic foraminifers. Radiolarians and diatoms are then often the only means of dating such sediments. In areas outside of the equatorial regions of high productivity (about 5° N to 2° S) sediment accumulation rates are relatively low, and as shown here, dissolution within the upper 30 cm of sediment can effectively remove all but the

most resistant species. Reworked Tertiary radiolarians are common in tropical Pacific sediments north of the Clipperton Fracture Zone^{6,7}. Where younger indigenous forms have been selectively removed, the older more resistant Tertiary radiolarian may dominate the microfossil assemblage. Other investigators^{8,9} have suggested this conclusion before, but to our knowledge this is the first time close interval sampling and measurements have been made that clearly establish the role of dissolution in creating apparently Tertiary 'age' in otherwise younger sediment.

Another way of estimating the age of the sediment, on a gross scale, is by the percentage of smectite in the clay fraction. Apparently, in northern equatorial Pacific sediment, Tertiary material is relatively high in smectite (60–80%) whereas the smectite content of Quaternary material is in the range of 20–40% (refs 10, 11). It is not clear whether this difference represents a diagenetic reaction involving assimilation of dissolved silica or a change in the source of the clay material. In any event, the low smectite concentration over the full core length suggests that despite the apparent Tertiary assemblage of microfossils, the material is of a more recent age. This finding suggests that selective dissolution of microfossils can lead to a sediment having an apparent biostratigraphical age which is not compatible with observed isotopic and mineralogical information.

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Biogeography and the caves of Bermuda

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Recent investigations of the more than 100 inland marine caves of Bermuda have shown that the number of invertebrate species inhabiting them is large, the amount of endemism is greater than one might expect, and the biogeographical relationships among species of certain genera encountered suggest more than one route of colonization. We believe that some of Bermuda's cavernicolous invertebrate marine fauna originated from stocks transported from the Caribbean via the Gulf Stream; some may represent groups that survived on submerged and emergent sea mounts along the Mid-Atlantic Ridge since the middle Mesozoic; some are relict deep sea fauna, while others may be Tethyan relicts. In addition, we hypothesize that the geothermal temperature gradient, observed as shallow as 30 m below present sea level¹, may have maintained water temperatures in some caves sufficiently high to protect certain groups during Pleistocene glaciation.

The inland marine caves of Bermuda contain a rich and diverse invertebrate fauna². The cave decapods include a new genus of hippolytid shrimp (*Somersiella sterreri*) and a new species of Atyidae (*Typhlatya iliffei*), as well as *Barbouria cubensis* (von Martens), *Barbouria antiquensis* Chace and four other shrimps³. The relationships of the ranges of several of these species to those of their allies are puzzling: the closest relative of *T. iliffei* is *T. rogersi* Chace and Manning, known only from Ascension Island in the south central Atlantic; *S. sterreri* is probably related to *B. antiquensis*, but differs from it in many respects; and *B. antiquensis* has been known previously only from the type-locality on Antigua. The hippolytid genera *Barbouria* and *Somersiella*, with their related genus *Ligur* from the eastern Atlantic and the Indo-West Pacific, may be Tethyan relicts. In addition to the decapod discoveries, representatives of a new order of the superorder Peracarida have simultaneously been discovered in several of the Bermuda caves and in the deep sea from 1,000 m depth off the coast of Surinam⁴.

Besides these biological finds, subsurface water temperatures recorded from pools in the deep cave interior were found to remain nearly constant all year round. Additionally, temperature profiles in those Bermuda caves most remote from the sea show small but significant increases with depth (Fig. 1), perhaps an extension of the natural geothermal gradient observed in the underlying basalts¹.

These discoveries have led us to speculate on the origins of some members of the Bermuda cave fauna, and the possibility that the survival of organisms in Bermuda caves over long periods of time is enhanced by moderate and stable temperature conditions.

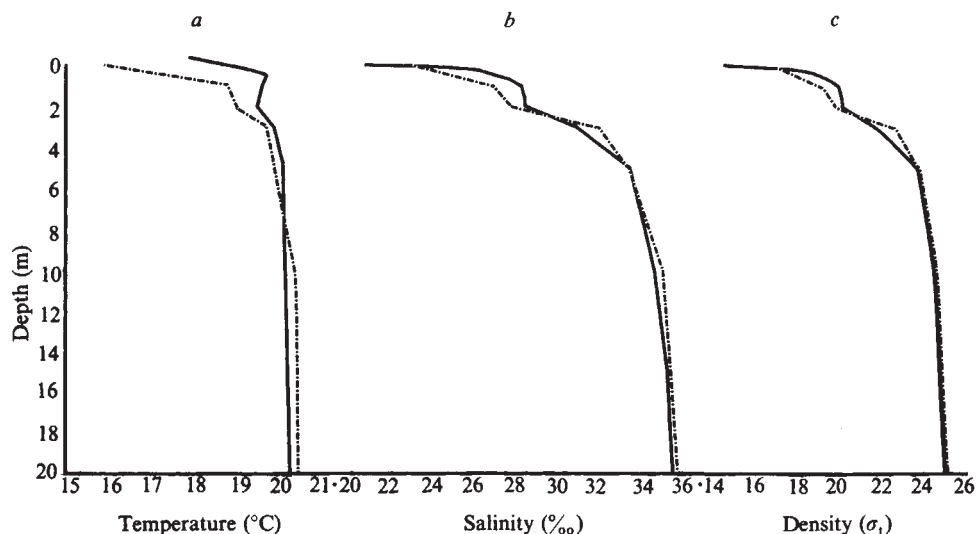
Bermuda was formed by a volcanic eruption along the Mid-Atlantic Ridge ~100 Myr BP (ref. 5), at which time Bermuda was at its closest proximity to the Eastern Hemisphere. During the late Cretaceous to early Tertiary periods (100–60 Myr BP), the top of the Bermuda seamount was probably submerged to such depths that a shallow water habitat did not exist (J. M. Peckenhams, personal communication). About 30 Myr ago, a second phase of volcanism began. During the early Pleistocene, the volcanic platform was eroded to its present average depth of ~75 m below present sea level. Bermuda's limestones, which completely cap the volcanic platform, are primarily eolianites, deposited during interglacial high stands of Pleistocene sea level. The deepest known carbonates are ~75 m below sea level and are probably early Pleistocene in age⁶. The island's caves and karst are believed to have a syngenetic origin, and thus have existed since the early Pleistocene^{7,8}.

We can hypothesize that the origin and evolution of Bermuda's cave fauna was at least partially controlled by the geological history of the island and that dispersal processes may have been significantly affected by various events in the island's history. As the immigration rate for an island decreases with distance from the source region⁹, only shortly after its formation would Bermuda have been close enough to the Eastern Hemisphere for most dispersal processes to be effective. Although Bermuda is a relatively old oceanic island and occupies an isolated position in the North Atlantic, its littoral fauna shows a comparatively low level of endemism—indicating a lack of genetic isolation. The Gulf Stream has presumably been the major factor accounting for this lack of isolation as is indicated by the large percentage of Bermuda's shallow water fauna that is of Caribbean origin¹⁰.

Although Bermuda's littoral fauna has direct connections with the Caribbean via the Gulf Stream, its cave fauna is probably considerably more isolated: the caves represent small 'islands' within a small island. Evidence supporting the greater isolation of the cave fauna is the recent discovery of at least 24 new cavernicolous invertebrate species. This represents a 30% endemism among the cave fauna, with the number of endemic species appearing to increase with distance into the cave interiors.

The idea that the caves have served as isolated refuges for certain species at least since the early Pleistocene appears highly

Fig. 1 Temperature (a), salinity (b) and density (c) profiles in Church Cave, Bermuda as measured on 28 February 1982 (broken line) and 11 July 1982 (solid line). The inshore water temperatures on those dates were 17.3 and 27.9 °C, respectively. Humidity in the deep cave interior is nearly 100%. Consequently, due to the lack of significant evaporative cooling, air and surface water temperatures in the caves are nearly equal. The cooler surface water may be due to the predominance of fresh water recharge in the winter months when surface evapo-transpiration rates are lower. The absence of seasonal changes in the cave water column below ~3 m indicates that the deeper cave waters are well isolated from the open sea. Although the tidal range in Church Cave is 40% that of the surrounding ocean and has a lag of ~107 min, the distance between the cave pool and the nearest open water, ~300 m away, is apparently great enough so that little net exchange of water occurs. A geothermal temperature gradient has been observed in volcanic rocks as shallow as 30 m below sea level¹. It is possible then that the deeper waters in isolated, inland caves of Bermuda may be maintained at near constant temperatures by geothermal heat flow into this meromictic environment.



attractive, particularly in light of the moderate and stable water temperatures noted in the caves. Today, Bermuda is near the oceanic winter isotherm of 20 °C (although inshore winter water temperatures often drop to 15 °C) and, because of this, has the northernmost coral reef ecosystem in the Atlantic Ocean. During periods of Pleistocene glaciation, lower winter water temperatures (by ~2 °C)¹¹ probably caused the extinction of many tropical species¹². Assuming that this 2 °C drop also applies to the deep cave water temperatures, they would have been ~18–20 °C, still ~3–5 °C warmer than inshore winter water temperatures today. If the geothermal gradient actually does provide a significant contribution, cave waters would have been even warmer.

The question arises as to what the maximum age for representatives of Bermuda's present fauna might be. It is unlikely that a shallow water habitat existed continuously on Bermuda until the beginning of the second phase of volcanism, ~30 Myr BP (Miocene). Although those eruptions were probably not especially violent, the local environment still would not have been conducive to the survival of most organisms. Thus, it appears at first to be unlikely that any species existing on Bermuda today predates the termination of volcanism, at least not in a continuous occupation.

Perhaps cavernicolous species colonized the island and lived in anchialine pools or lava tube caves on post-volcanic Bermuda until the formation of limestone caves in the early Pleistocene. Similar habitats supporting cavernicolous faunas exist today on other volcanic oceanic mounts^{13–16}.

Changes in the sea level during the Pleistocene profoundly affected the cave habitats. Pleistocene low sea stands were at least 85 m below present sea level¹¹, such that the top of Bermuda's volcanic pedestal was no longer submerged. The deepest caves explored on Bermuda reach depths of 25 m below present sea level, although we suspect that deeper caves may exist near the limestone-basalt interface.

Although all known portions of Bermuda's submerged caves were dry for prolonged periods during glacial low stands of sea level, it is highly unlikely that the establishment of such a rich endemic marine cave fauna postdates the last major glacial period, which occurred only 18,000 yr ago¹¹. It is possible that deeper cave systems along the flanks of the volcanic cone contained marine waters and thus may have provided a temporary habitat for the cavernicolous fauna. The slow rise and fall of sea level during the Pleistocene (~3 mm yr⁻¹)¹⁷ would have provided ample time for the fauna to migrate to adjacent caves in Bermuda's highly integrated cave network.

However unlikely it may seem that species existing on Bermuda today could predate the termination of volcanism, the implications of the presence there of *T. iliffei* should not be overlooked. Species of the genus *Atya* may have existed in a comparatively stable state since at least early Cenozoic times—perhaps since the middle Mesozoic—and their probable monophyletic origin may predate a very wide separation of the African and American continental masses¹⁸. If this is true, then we might suppose that the closely related *T. iliffei* (on Bermuda) and *T. rogersi* (on Ascension) represent an atyid stock that originated at about the same time and place as did the genus *Atya*, surviving on submerged and emergent sea mounts along or associated with the Mid-Atlantic Ridge.

Thus, we believe that the cave shrimps of Bermuda (and, by extrapolation, other invertebrates as well) have had at least three temporal derivations: (1) recent (*B. cubensis* and *B. antiquensis* from the Caribbean via the Gulf Stream); (2) during the separation of the African and American continental masses (*T. iliffei*); and (3) from Tethyan relicts (*S. sterreri*). Additionally, some cave invertebrates are probably of deep sea origin.

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Acoustic distance discrimination by the cod

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Recent experiments have shown that the cod, *Gadus morhua* L., is able to determine the direction of a sound source without ambiguity in three-dimensional space^{1,2}. This ability can be explained in terms of the detection of particle acceleration by the otolith organs of the labyrinth, which are strongly directional in their response to oscillatory motion^{3,4}. Ambiguities in determining the direction of propagation are resolved by the fish detecting phase differences between the particle acceleration and the sound pressure^{2,5}. The phase relationship between these two quantities varies with distance from a source, and might therefore provide distance cues to the fish^{2,6}. We now report an experiment performed in the field which confirms that cod can discriminate between pure tones emitted alternately from two aligned sound projectors at different distances. Our results suggest that the cod is well able to locate low-frequency sound sources in three-dimensional space.

Cod, like many other fish, are acutely sensitive to low-frequency underwater sounds⁷ (below ~500 Hz). Moreover, directional hearing has now been demonstrated in this fish and is mediated by the paired labyrinths; the lateral line system need not be implicated^{2,8}. In mammals, the direction of a source is determined by the analysis of disparities in the phase, time of arrival and intensity at the two spaced ears. The speed of propagation of sound through water is higher than in air (by a factor of 4.5), and differences in the phase and time of arrival of a sound at the ears of a fish are correspondingly smaller. In addition, the head of a fish is effectively acoustically transparent, reducing any sound shadowing and minimizing intensity differences between the ears.

The pressure wave which characterizes a sound is also accompanied by an oscillatory acceleration of the water particles about their equilibrium position along the line from the source. The otolith organs of the fish labyrinth respond to the particle acceleration and serve as vector component detectors^{3,4}. Such a system of vector detectors alone is not capable of determining the direction of propagation of a sound. The instantaneous particle motion is alternately opposite and common to the direction of propagation, and a simple particle motion detector is therefore inherently bidirectional. It has been shown that comparison of the phase of particle acceleration and sound pressure enables the fish to determine the direction of propagation without ambiguity^{2,5,8}. Cod are capable of discriminating much smaller phase differences between particle acceleration and sound pressure than the 180° required for unambiguous directional detection^{2,6}. The actual differential phase threshold is about 15° at 120 Hz (R. J. A. Buwalda, P. Boeijinga, D. J. Wester and A. S., unpublished results). The phase relationship between the two quantities is known to vary with distance from a sound source⁹, as shown in Fig. 1. An ability to resolve small differences in phase might therefore enable the cod to determine source distance. On the basis of the thresholds obtained, the fish should, for example, be able to discriminate a source at 0.5 m from one at 1.0 m, and one at 4.0 m from one at 7.0 m.

We have recently examined cod for evidence of distance perception. From an experimental standpoint, the ability is most readily demonstrated in a free sound field, with spherically

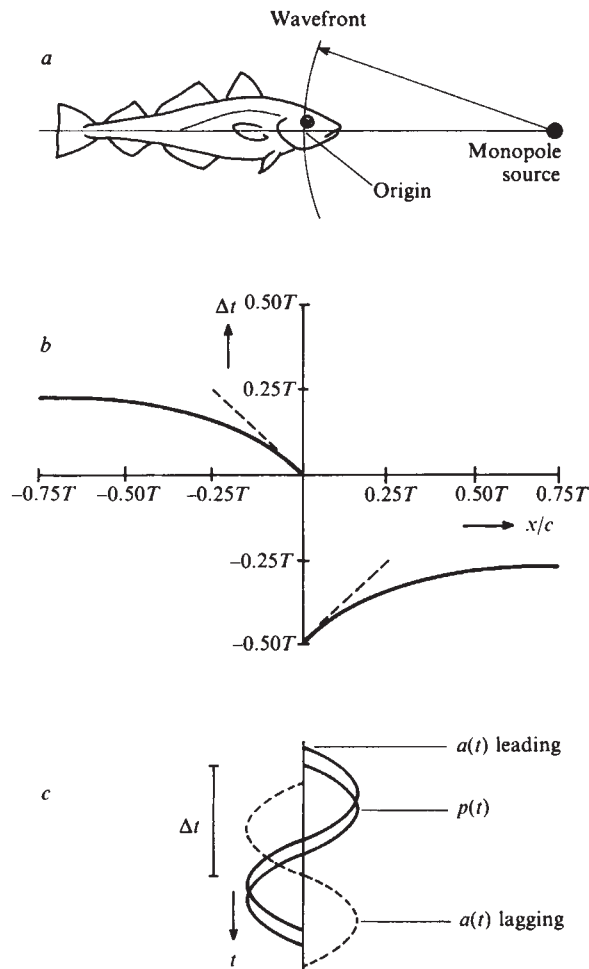


Fig. 1 The phase relationship ψ between particle acceleration $a(t)$ and sound pressure $p(t)$ in a diverging spherical wave is a function of the distance from the source⁹. In the figure it is expressed as a time difference Δt between a rostrad-directed zero crossing of $a(t)$ and a positive-going zero crossing of $p(t)$. Position is expressed as the distance to the source x , divided by the velocity of sound c . **a** Shows the origin of the body fixed coordinate system at the ear of the fish. In **b** both Δt and x/c are given in units of the period T of the oscillations. For sinusoidal sounds $\psi = 360^\circ x/cT$. The relationship is valid for non-sinusoidal waveforms, provided the highest spectral components satisfy the condition $x/c < T/4$. The graph consists of two distinct parts on either side of the origin, denoting sound sources in rostrad and caudad positions. The signal $a(t)$ shows a phase reversal from one position to the other. This reversal is shown in **c**, where leading and lagging $a(t)$ waveforms are drawn. The interval Δt is shown between $p(t)$ and the lagging $a(t)$.

spreading sound waves. These conditions are impossible to obtain in the laboratory, and our experiments were therefore conducted with the fish and sound projectors suspended in midwater in the sea. A site was chosen in a Scottish sea loch with a water depth of 25–30 m (depending on the tide), and the fish, sound projectors and hydrophones placed 10 m below a raft. The fish, with cardiac electrodes attached, was confined within an optically opaque, acoustically transparent cage facing a line of three sound projectors 1.3, 4.5 and 7.7 m away in the horizontal plane. A sound pressure hydrophone and two velocity hydrophones (one with a horizontal axis parallel to the sound projectors, the other with a vertical axis) were mounted above the head of the fish (Fig. 2). Before the experiments began, the amplifiers driving the sound projectors were adjusted to give

the same sound pressure level (2 dB at 1 Pa) at the head of the fish for the same input signal.

The sound projector at 4.5 m emitted a continuous train of tone pulses. The 112.5 Hz pulses were 850 ms long with a gradual rise and fall, and were separated by 150 ms of silence. Their amplitude was varied randomly within a 6 dB range. This train of pulses served as a neutral signal to which the fish was habituated. The fish was then trained by cardiac conditioning to respond to an alternate switching of the sound between this projector and the closer one. The switching was under electronic control and took place during the silent period between successive pulses. A series of five alternations between the two projectors provided the conditioned stimulus, which was always followed by a mild electric shock. Subsequently, the train of pulses reverted to the projector at 4.5 m. A conditioned response to the alternation of pulses between projectors was established in about 10 trials, and consisted of a pronounced slowing of the heart beat.

In addition to the conditioned stimulus, a probe stimulus was presented intermittently, and consisted of a similar alternation between the 4.5 m projector and the distant projector, without shock being administered. This stimulus was intended to establish whether the fish responded by generalizing to a different change in distance without reinforcement. Blank trials were occasionally interpolated and consisted of an electronic switching of the apparatus without any change to the projector, followed by shock. These trials served as checks for unintended cues.

Experiments were performed on two cod on separate occasions. The Wilcoxon paired sample test was applied to test whether the fish detected the changeover from one projector to another. For each trial, the difference between the maximum cardiac interval during the period of alternation and the maximum interval in an immediately preceding pre-trial period of equal duration was calculated. Under the null hypothesis, the mean population difference will be zero when the alternation has no effect on the heart beat.

The responses of the fish to both the conditioned stimulus and the probe stimulus were pronounced. Both samples were significant at the 0.05 level ($n=48$, $P<0.0001$ and $n=11$, $P<0.001$, respectively). Although the probe stimuli were not reinforced, there was no evidence of habituation to them. The fish did not respond to the blank trials.

We were unable to test whether the sound projectors themselves were different in timbre, providing an unintended cue to the changeover. However, the sound projectors (USRL, type J9) were carefully matched, and an observer listening on the sound pressure hydrophone was unable to detect the alternation between one projector and another.

We conclude that cod can discriminate between short tone pulses emitted alternately by two sound sources at different distances. This conclusion is supported by a recent finding (R. J. A. Buwalda, P. Boeijinga, D. J. Wester and A. S., unpublished results) that the masked threshold for cod to tones is lower when a narrow band noise masker is simulated to come from a different distance to a tone stimulus, showing that the cod is capable of filtering sounds by means of distance-dependent cues.

Although we suggest that the cod discriminates sound source distance by means of relative phase cues, there are several other possible cues. Close to a source the amplitude ratio between sound pressure and particle velocity changes with distance (the 'near-field effect'). The change in velocity amplitude for a constant sound pressure would be less than 4 dB with our experimental stimulus. Such amplitude differences may be below the threshold for detection by cod¹⁰, and are unlikely to have provided the only cue to distance. The relative amplitudes of the vertical and horizontal components of particle acceleration may also differ with distance, but again these differences are small. Characteristic patterns of amplitude modulation may be generated at different distances as a result of the reflection of sound by the sea bed and surface, and we believe that these

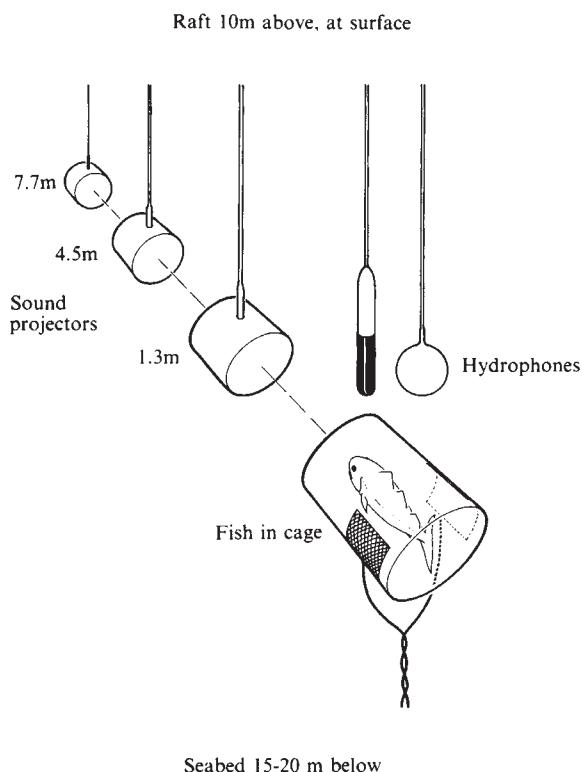


Fig. 2 The acoustical arrangements for demonstrating acoustic distance perception by cod. Three sound projectors were hung at the same depth beneath a raft, at different distances from the fish, which was confined in an acoustically transparent cage. A sound pressure hydrophone, and two particle velocity hydrophones monitored the sound stimuli. Both velocity hydrophones were contained within the same spherical housing, one orientated along the line of the sound projectors with its axis in the horizontal plane, the other with its axis orientated vertically.

effects may be important in providing distance cues far from a source.

If the observed discrimination is based mainly on relative phase cues, as we suggest, it is quite likely that the cod is able to estimate the true distance of a sound source in its vicinity. Combined with its three-dimensional directional hearing capabilities, this would provide the cod, an animal living essentially in a three-dimensional habitat, with a real acoustical sense of space. In this respect the auditory capacities of cod would far exceed those of most terrestrial vertebrates.

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Nutrition and lactational control of fertility in red deer

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In many mammals, including man, lactation is associated with a delay in return of fertility. The pattern of suckling activity, particularly suckling frequency, is known to be important in determining the length of this anovulatory phase^{1,2}. In a seasonally breeding ungulate such as red deer, lactation coincides with a photoperiodically controlled period of seasonal anoestrus³. Nevertheless, lactation may still exert an important effect on the duration of infertility as lactating red deer hinds on poor quality hill pasture resume oestrus at a later date than non-lactating hinds and frequently fail to ovulate in the year following the birth of a calf^{4,5}. It has been proposed that this reproductive failure is due to the effect of both lactation and poor planes of nutrition on maternal body condition⁶⁻⁸. As a result of our recent studies on the influence of plane of nutrition on milk yield and suckling behaviour in red deer we now propose an alternative hypothesis. We suggest that the principal influence of low planes of nutrition is to increase the suckling frequency of the calf in response to a decrease in availability of milk. It is this increase in suckling frequency, and perhaps the associated increase in plasma levels of prolactin, which is the major determinant of the reproductive failure and is due to the influence of plane of nutrition on the production of milk by the mother rather than on maternal body condition. This hypothesis may have important implications for our understanding of the role of nutrition in determining the length of lactational infertility in many species including man.

Seventeen red deer hinds (8 or 9 yr old; 75–90 kg body weight) which had been kept on a hill pasture with supplementary hay throughout pregnancy were randomly allocated to one of two treatment groups at the time of calving. Nine hinds were placed in a paddock of permanent grass maintained in a vegetative state at 1,800 kg dry matter per hectare and with a mean sward digestibility of 69%. The other eight hinds were placed in a paddock of hill pasture dominated by dwarf shrubs and indigenous grasses of low density and quality with a mean

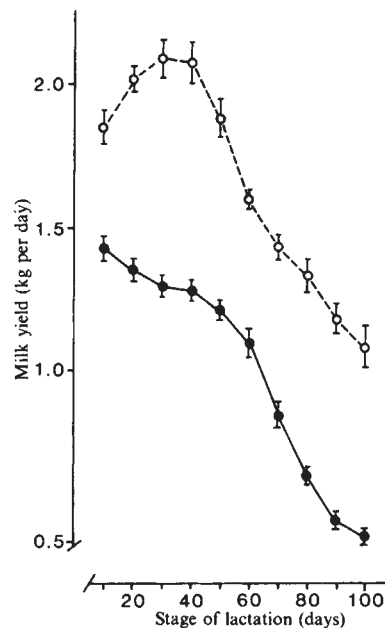


Fig. 1 Mean milk yields ($\pm$ s.e.m.) of red deer hinds on hill (●) and permanent grass (○) throughout lactation. Hinds were collected from the pasture, separated from their calves, and a blood sample (15 ml by jugular venipuncture) collected from manually restrained hinds within 30 min of the gathering. Subsequently, milk yields were estimated by the weight difference ($\pm$ 5 g) of the calf before and after suckling at 6-hourly intervals over a 24-h period. Plasma samples were stored at -20°C until assayed using a heterologous radioimmunoassay described in detail previously²¹. Both groups of hinds were separated from their calves on 15 September at $\sim$ 110 days of lactation and placed in a single group for breeding with one stag.

digestibility of $\sim$ 60%. This pasture had a complex effect on the grazing activity of the lactating hinds which resulted in a significant reduction in overall food intake⁹. Milk yields were estimated over 24-h periods at 10–14-day intervals throughout lactation as described in Fig. 1 legend.

Hinds on the permanent grass pasture had significantly higher (about 1.6 times) milk yields than those of hinds on hill pasture (Fig. 1). Despite these differences in lactational performance, there were no significant differences in body weight of the hinds (Table 1). However, the reduced milk yields of the hinds on hill pasture was associated with a significant reduction in the weight gain of the calves throughout lactation (Table 1).

Plasma levels of prolactin were significantly higher in the hinds on the hill pasture although in both groups mean prolactin levels declined throughout lactation in response to declining daylength (Fig. 2) as shown previously¹⁰. Further, while prolactin levels in each group were significantly correlated with milk yield (Fig. 2) it was clear that for any given level of milk yield, hinds on improved pasture had significantly lower prolactin

Table 1 Changes in body weight (mean $\pm$ s.e.m.) of red deer hinds and calves throughout lactation for group on indigenous hill ($n=8$) or permanent grass pasture ($n=9$)

Stage of lactation (days)	Body weight (kg)		Calf	
	Hind*		Calf	
	Hill pasture	Permanent pasture	Hill pasture	Permanent pasture
0	—	—	7.9 $\pm$ 0.4	7.8 $\pm$ 0.3
10	84.9 $\pm$ 1.3	83.5 $\pm$ 2.2	11.7 $\pm$ 0.5	11.6 $\pm$ 0.3
20	83.4 $\pm$ 2.4	82.3 $\pm$ 1.6	15.4 $\pm$ 0.8	15.8 $\pm$ 0.4
30	83.5 $\pm$ 2.6	85.2 $\pm$ 2.1	18.3 $\pm$ 0.9	19.0 $\pm$ 0.5
40	84.5 $\pm$ 2.6	88.4 $\pm$ 2.6	21.1 $\pm$ 0.9	22.6 $\pm$ 0.6
50	85.6 $\pm$ 2.4	87.5 $\pm$ 2.1	23.6 $\pm$ 0.9	26.5 $\pm$ 0.7
60	85.6 $\pm$ 2.6	87.3 $\pm$ 2.1	26.3 $\pm$ 1.0	29.9 $\pm$ 0.7
70	86.7 $\pm$ 2.6	89.4 $\pm$ 2.4	29.1 $\pm$ 1.0	33.6 $\pm$ 0.7
80	87.4 $\pm$ 2.7	91.2 $\pm$ 2.3	31.6 $\pm$ 1.1	37.6 $\pm$ 0.8
90	87.3 $\pm$ 2.7	92.0 $\pm$ 2.1	34.1 $\pm$ 1.2	41.4 $\pm$ 0.9
100	88.7 $\pm$ 2.8	92.8 $\pm$ 2.2	36.2 $\pm$ 2.1	44.7 $\pm$ 0.9

* No measurements were made on the day of calving.

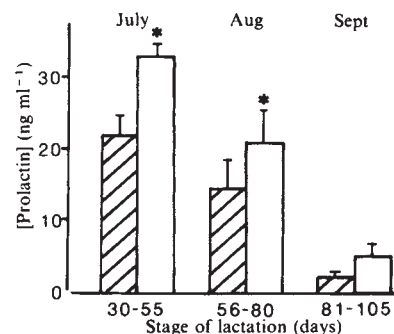


Fig. 2 Relationship between plasma levels of prolactin (mean $\pm$ s.e.m.) and stage of lactation for red deer hinds on hill (□) and permanent grass (▨) pastures.

Table 2 Pattern of suckling activity by calves of red deer hinds on hill and permanent grass pasture at different stages of lactation

Group	Stage of lactation (days)								
	40-60			61-80			81-100		
	No. of suckling bouts	No. of rejects	Suckling time per day(s)	No. of bouts	No. of rejects	Suckling time per day(s)	No. of bouts	No. of rejects	Suckling time per day(s)
Hill pasture	4.2±0.7	5.0±0.6	304±27	4.1±0.9	2.4±0.7	275±62	3.6±0.8	3.0±0.6	201±49
Permanent grass pasture	1.9±0.3	0	837±42	1.5±0.5	0.6±0.1	808±51	1.4±0.7	0	623±77

Results include the number of successful suckling attempts and their total daily duration, and the number of attempted sucklings which were rejected by the mother. All observations reported were made between 05.00 and 22.00. A limited number of observations made between 22.01 and 04.59 using an image intensifier suggested that suckling during the hours of darkness is very uncommon.

levels than hinds on hill pasture (Fig. 3). These differences in prolactin levels were completely unexpected and are in contrast with results in non-lactating cattle and sheep where animals on low planes of nutrition have significantly lower plasma levels of prolactin than those on high planes of nutrition¹¹.

As the level of prolactin in lactation is related to the frequency and intensity of the suckling stimulus, with high suckling frequencies inducing increased prolactin secretion², our prolactin results suggested that the plane of nutrition might be affecting the suckling pattern of the calves in the two groups. Observational data confirmed this and showed that the differences in milk yields were associated with a dramatically different pattern of suckling activity by the calves in the two experimental groups. Not only did calves on low quality hill pasture suckle more frequently for short periods but they frequently attempted to suckle and were rejected by their mothers throughout lactation. In contrast, calves on improved pasture suckled infrequently but for longer, and suckling attempts were rarely rejected by their mothers (Table 2). Thus, although the overall pattern of prolactin release throughout the year is principally influenced by daylength in red deer¹⁰, our data show that suckling frequency has an additional modifying influence on prolactin levels even when these are increased in seasonal anoestrus (Fig. 2).

These results provoke the question, why did the calves of low yielding mothers suckle more frequently? One important reason may be the amount of milk available in the mammary gland at any one suckling time and this is dependent on the fill rate of the mammary gland. Sedation and machine milking¹² of our hinds at 4-hourly intervals indicated that the mammary glands of the hill pasture group filled at half the rate of those of hinds on the permanent pasture ($18.0 \pm 3.2 \text{ g h}^{-1}$ compared

with $39.6 \pm 2.7 \text{ g h}^{-1}$ (mean $\pm$ s.e.m.), $P < 0.01$; at mid-September). Thus, at any one time less milk is available to the suckling calf on hill pastures and, in an attempt to obtain adequate milk intake to maintain growth at its genetic potential, the calf returns to the mother at frequent intervals. Indeed, the calves returned more frequently than mothers would allow them to suckle therefore the rejection rate per attempted suckling was considerably higher than in the permanent pasture group with higher milk yields (Table 1).

All the available evidence suggests that suckling frequency is of major importance in maintaining increased prolactin secretion and the control of the duration of infertility associated with lactation^{1,2,13}. Suckling duration only becomes important as suckling frequency declines¹³. In our study the hinds in the improved pasture group returned to oestrus significantly earlier than the hill group (+6.2 days, $P < 0.05$) suggesting that the pattern of suckling activity by their offspring had an important modifying influence on the resumption of breeding activity following seasonal anoestrus. It is interesting that in the study of wild red deer on Rhum, hinds which supported male calves with a higher suckling frequency returned to oestrus 11 days later than those suckling female calves¹⁴.

The implications of our studies may also be important with regard to breast feeding and the human birth interval. Whether prolactin *per se* is ultimately involved in the control of fertility in any species remains unknown^{2,15}. However, it is clear that in women the duration of lactational infertility and amenorrhoea is directly related to the intensity of the suckling stimulus^{2,15-17} which in turn controls the level of prolactin. Fertility returns post partum when the suckling stimulus diminishes^{15,17}. The influence of nutrition on the duration of lactational amenorrhoea in women, and hence the interbirth interval, is also a matter of conjecture^{18,19}. However, most evidence suggests that overt malnutrition has only a minor role in maintaining lactational amenorrhoea¹⁸. Significantly, however, it has been shown that improving the maternal diet by giving a high protein biscuit to the mother resulted in a reduction in plasma prolactin levels and an earlier resumption of fertility in breast-feeding mothers in the Gambia²⁰. However, although this study suggests that the improved maternal nutrition did not affect the pattern of suckling in these women, this has not been fully evaluated (R. Whitehead, personal communication). Our data suggest that, within a species, the pattern of suckling activity by the offspring is highly variable and suckling frequency depends not only on the requirements of the suckling offspring but also on the availability of milk, which, in turn, depends on the nutritional state of the mother. Thus in both seasonal and non-seasonal breeding mammals, including man, it is possible that the influence of maternal nutritional state on the resumption of fertility during lactation is more directly related to its impact on the suckling activity of the offspring than to the maternal nutritional status *per se*.

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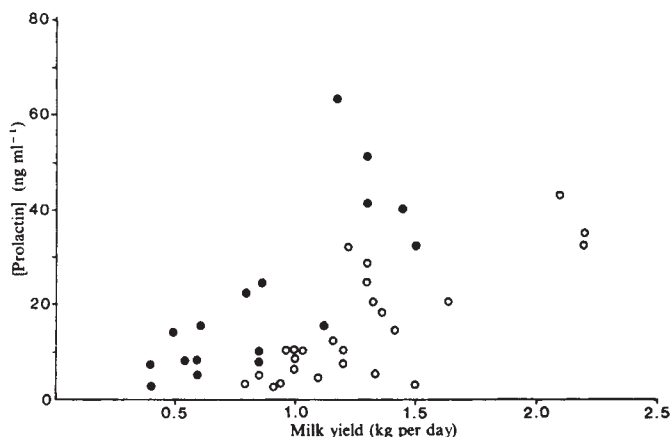


Fig. 3 Relationship between milk yield and plasma levels of prolactin for red deer hinds on hill (●) and permanent grass (○) pastures throughout lactation. Regression equations: hill pasture group, $y = 0.039x - 11.92$, $r = 0.79$, $P < 0.01$; permanent grass pasture group, $y = 0.023x - 14.70$, $r = 0.79$, $P < 0.01$.

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Genetic kin recognition: honey bees discriminate between full and half sisters

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The ability of organisms to recognize kin not previously encountered has been demonstrated in monkeys¹, mice², frogs^{3,16}, a sweat bee^{4,5} and the honey bee⁶. The environmental and genetic components of recognition are difficult to separate even in controlled conditions. Here we show that the honey bee *Apis mellifera* discriminates between full and half sisters raised in the same hive, on the same brood comb in neighbouring cells, thus demonstrating a significant genetic component to the recognition process. Besides its ethological implications, this work has implications for the evolution of sterile worker castes in hymenopterans⁷⁻¹⁰.

Queen honey bees mate with a number of different drones before they lay their first eggs¹¹. The sperm, to some extent, mix in the spermatheca and the hive contains several distinct patrilineal worker groups of full sisters while the workers are matrilineal half sisters across groups^{12,13}. In Hymenoptera, males develop from unfertilized haploid eggs and females develop from fertilized diploid eggs. Consequently, worker bees are three times more closely related to their full ($r = 3/4$) than half sisters ($r = 1/4$)^{14,15}. Hamilton⁷, using a genetic model, derived the principle that an individual can enhance its inclusive fitness by altruistic acts towards its kin, especially its close relatives. In honey bees, where full sisters are so closely related, the individuals of the 'dominant' (numerically, aggressively or otherwise) patrilineal worker group could enhance their fitness by raising a full sister as the new queen that supersedes the old queen or replaces the old queen when the colony swarms. Nonrandom segregation along patrilines during swarming has been observed⁹. If this behaviour is related to the preferential association of kin groups, then kin recognition at the intra-colony level is implicated. We investigated recognition at this level as follows.

Three hives were set up⁹ by instrumentally inseminating a queen with semen from two unrelated drones using genetic

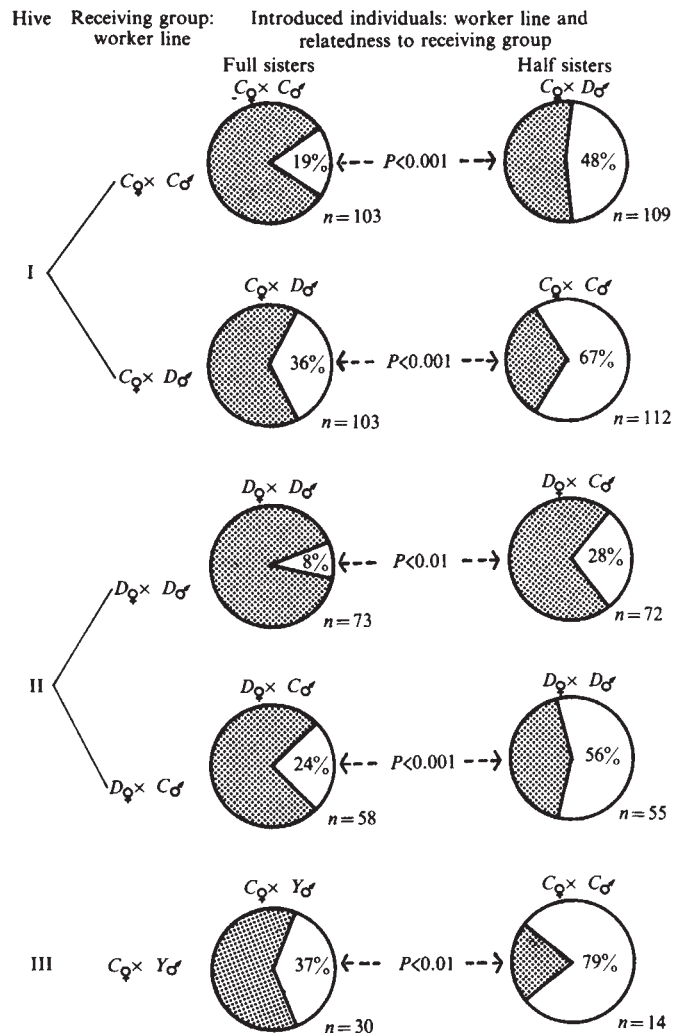


Fig. 1 Per cent of introduced individuals bitten by at least one member in the receiving group. The symbols n and P respectively denote sample size and significance level (χ^2 contingency table analysis). Worker lines were obtained by instrumentally inseminating cordovan (a light brown cuticle colour mutant denoted here by C) and dark coloured (derived from Carniolan stock and denoted here by D) queens with semen from cordovan, dark and yellow (derived from Italian stock and denoted here by Y) drones. Hives I, II and III were obtained from two drone inseminations yielding worker patrilines that are distinguishable on the basis of colour. In hive III, the $C_Q \times C_Q$ line was not tested owing to the death of its queen and a skewed worker emergence ratio in favour of the $C_Q \times Y_Q$ workers. Each group of 10 full sisters (mortality reduced the average size to 9.4 individuals), set up as discussed in the text, had either a single full or half sister introduced to it on day 5 and again on day 6. Introduced bees were only used once and recipient groups were used not more than once on either of the 2 days. Behaviour was observed for 5 min after each introduction at which point the introduced bee was removed. We then recorded whether the introduced bee was bitten by any of the bees in the recipient group. Data from the fifth and sixth days were pooled after it was determined that the overall lower level of the biting behaviour recorded on day 6 did not differ significantly from the level on day 5 ($P > 0.1$, χ^2 contingency table analysis). The data also indicate a significantly higher level of biting behaviour in the cross-bred lines ($C_Q \times D_Q$ and $D_Q \times C_Q$) than the 'pure' lines ($C_Q \times C_Q$ and $D_Q \times D_Q$) in hives I and II ($P < 0.05$ for all four within hive full-sister and half-sister comparisons).

lines that express distinguishable colour morphs in worker bees (Fig. 1 legend). Once the queen began laying, her colony was transferred to a four-frame observation hive. Three to five times a week for several months, 100 to 200 bees were removed within 24 h of their expected emergence from their capped cells. Individuals belonging to the same full-sister group were then isolated in groups of 10 in 0.455-litre cylindrical cardboard containers and maintained in an incubator at 31 °C on a diet of pollen substitute and sugar water. On the fifth and sixth days, following Breed⁶, the workers in one of these groups of full sisters were individually introduced into the remaining groups (Fig. 1).

The results indicate that workers are significantly more likely to bite half sisters than full sisters ($P < 0.01$ in all cases) even though all bees in each experiment were raised (egg, larval and pupal stage) in the same hive in neighbouring cells. Thus workers are using genetically based labels (such as morphological characters and odours) to discriminate between their full and half sisters, but it is not clear whether this ability is based on habituation to the labels of the nine workers in their co-group or whether they use their own set of labels as a cue. At this stage, there is no evidence that bees discriminate between full and half sisters in the hive once they are habituated to both sets of workers. This question should ultimately be addressed by studying behaviour within the hive.

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Antibodies to epithelial desmosomes show wide tissue and species cross-reactivity

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Many workers regard cell adhesion as a highly specific phenomenon, believing that different molecular mechanisms are involved in the adhesion of cells of different tissues and different species. We believe that the evidence from cell behaviour is against this view and that cells share common adhesion mechanisms (for reviews see refs 1, 2); however, molecular evidence is lacking. As an approach to providing such evidence we have begun to study desmosomes, the cell-surface organelles responsible for strong intercellular adhesion in epithelia. We have raised antisera against each of five high-molecular weight (MW) desmosomal components. Having determined the specificity of our antisera by immunoblotting, we show here that each gives a staining pattern corresponding to the distribution of desmosomes in a range of tissues from different vertebrate species, demonstrating that desmosomal components are widely shared and highly conserved.

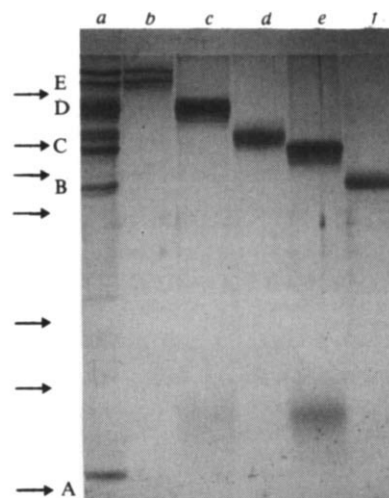


Fig. 1 10% Polyacrylamide slab gel showing desmosomal cores (lane a) consisting of: A, a 22K-MW glycoprotein; B, doublet of 82K and 86K proteins; C, a glycoprotein of 100K and a doublet glycoprotein of 115K; D, a triplet of glycoprotein of 150K; E, a doublet of 205K and 230K proteins. Lanes show purified desmosomal antigens. Desmosomal cores were isolated from cows' noses by the method of Gorbisky and Steinberg³ except that instead of a continuous metrizamide gradient, the crude cores were applied to a discontinuous gradient with steps of 50, 40, 30, 20 and 10%. After centrifugation at 180,000 g for 3 h the cores were collected from the 30–40% interface. They were dialysed into 0.1% SDS–5 mM β -mercaptoethanol overnight and then solubilized by boiling for 2 min in an equal volume of sample buffer. 2–3 mg of solubilized material were applied to each of three or four 7.5% slab gels and electrophoresed at 40 V overnight. Narrow strips were cut from one side of the gels and stained with Coomassie blue to locate the core proteins. The latter were isolated by slicing the respective areas from the unfixed gel and eluting in 0.05% SDS solution. The purity of the eluted proteins was verified by further slab gel electrophoresis (lanes b–f). Arrows denote marker proteins (Sigma, Pharmacia) from the top: myosin (205K), β -galactosidase (116K), phosphorylase b (94K), bovine albumin (67K), ovalbumin (43K), carbonic anhydrase (30K) and trypsin inhibitor (20K). Each antigen at a concentration of 200–300 μ g ml⁻¹ in 0.5% SDS was emulsified with an equal volume of Freund's complete adjuvant. Guinea pigs received 1 ml of emulsion distributed between two intramuscular sites in the back legs and two subcutaneous sites on the back. Two booster injections were given at 6–8-week intervals, the first with complete adjuvant, the second with incomplete. The animals were bled 7 days after the final injection.

Desmosomal cores were prepared from bovine nasal epithelium by a modification of the method of Gorbisky and Steinberg³ which was derived from the original procedure for desmosome isolation of Skerrow and Matoltsy⁴ (see Fig. 1 legend). Cores consist of five major groups of proteins as follows: A, a glycoprotein of MW 22,000 (22K); B, two proteins of MW 82K and 86K; C, a glycoprotein of 100K and a glycoprotein doublet of 115K; D, a glycoprotein triplet of 150K; E, two proteins of 205K and 230K^{3,5}. A, C and D are thought to be on the cell surface while B and E are thought to be plaque constituents^{3,5}. We have separated the components on 7.5% polyacrylamide gels (Fig. 1) and individually eluted a 86K, 100K, 115K doublet, group D and group E. The purity of these was checked by electrophoresis on 10% gels (Fig. 1) and the purified preparations were used to immunize guinea pigs (see Fig. 1 legend).

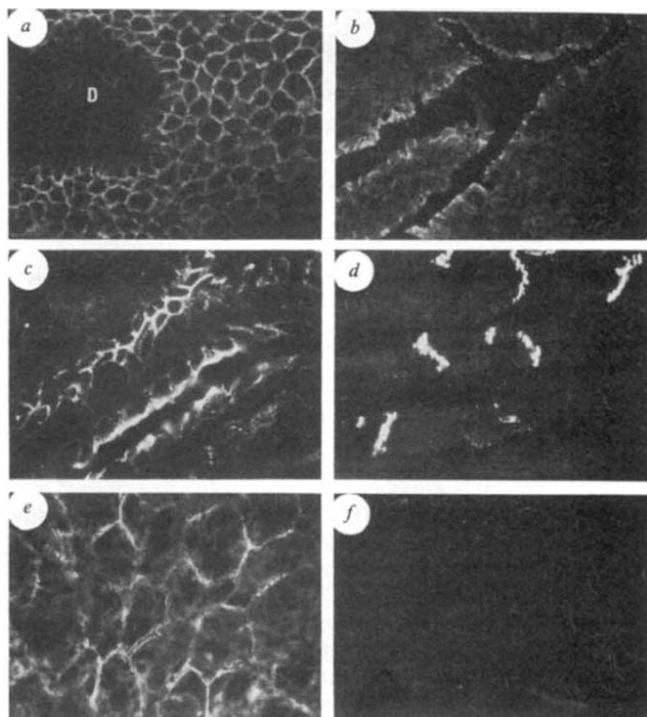


Fig. 2 Immunofluorescent staining of a variety of tissues from different animal species with anti-desmosomal antibodies, showing that staining patterns reflect the distribution of desmosomes and that staining is not tissue or species specific. *a*, Section of cow's nose stained with anti-110K. Note that the staining is confined to the cellular interfaces in the epidermis, is absent from the dermis (D) and is greatly reduced or absent from the dermal-epidermal interface. $\times 204$. *b*, Frog intestine stained with anti-205/230K showing bright staining of terminal bars and punctate staining elsewhere. $\times 204$. *c*, Rat stomach stained with anti-205/230K showing punctate staining of intercellular boundaries. $\times 730$. *d*, Rat heart stained with anti-205/230K showing specified staining of intercalated disks. $\times 330$. *e*, Rat liver stained with anti-205/230K showing punctate staining of bile canaliculi. $\times 330$. *f*, Rat skeletal muscle treated with anti-205/230 showing complete absence of staining. $\times 330$. All staining was carried out on $5\text{ }\mu\text{m}$ cryostat sections of freshly frozen material. The sections were first treated with the antiserum at a dilution of 1:40 in phosphate-buffered saline (PBS) for 30 min. They were then washed extensively with PBS (3 changes; 1 h) and treated with fluorescein-conjugated rabbit anti-guinea pig IgG (Wellcome) at a dilution of 1:20 in PBS. This was followed by a final wash in PBS for a minimum of 1 h and 3 changes. Slides were mounted in 9:1 glycerol-PBS and viewed by incident illumination on a Zeiss Photomicroscope III.

In each case the antisera obtained gave strong staining of the cell interfaces in the epidermis of the bovine nasal epithelium (Fig. 2*a*). Staining was often punctate, as would be expected from the concentration of desmosomes on the spinous, interdigitating processes of these cells^{3,4}, and was completely absent from the dermis in which there are no desmosomes. The pattern of staining obtained with antisera against the different antigens was identical. This would be expected, as the total thickness of a cow's nose desmosome from one cytoplasmic plaque to the other is less than 100 nm so that differences in distribution of antigens within desmosomes are below the resolution of the light microscope.

Immunoblotting experiments (Fig. 3) against desmosomal cores showed: (1) Antisera to E group proteins reacted strongly with the 205K and 230K components only. Franke *et al.*⁵ and Gorbisky *et al.*⁶ have shown that antibodies against these

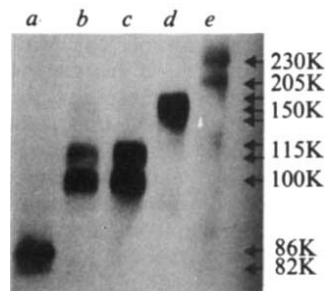


Fig. 3 Immunoblotting experiment performed with desmosomal cores separated on a 5–20% polyacrylamide gradient gel. Lane *a*, anti-86K showing cross-reaction with 82K; lane *b*, anti-100K showing cross-reaction with 115K; lane *c*, anti-115K showing cross-reaction with 100K; lane *d*, anti-150K and lane *e*, anti-205/230K. Arrows denote the positions of the core proteins. The gel was renatured according to the method of Risau¹⁵. Blotting onto nitrocellulose was then carried out overnight at 4 °C according to the method of Towbin *et al.*¹⁶. After staining a reference strip with amido black, the rest of the blot was cut into strips and blocked with 3% ovalbumin in Tris-buffered saline (0.9% NaCl, 10 mM Tris-Cl pH 7.4) for 1 h at 40 °C. A brief rinse in distilled water was followed by incubation with antibody diluted to 1:50 in 150 mM NaCl, 5 mM EDTA, 50 mM Tris-HCl (pH 7.4), 0.25% gelatin for 2 h at room temperature. Strips were briefly rinsed in the same buffer containing 0.05% Nonidet P-40, then incubated with ¹²⁵I-labelled protein A at 10⁶ counts per ml in the washing buffer for 2 h at room temperature. They were then washed in 1 M NaCl, 5 mM EDTA, 50 mM Tris-HCl (pH 7.4) 0.25% gelatin, 0.4% sarkosyl. Six changes were given over a period of 2 h. Strips were rinsed in water, air-dried and autoradiographed for 16–18 h.

Table 1 Summary of the staining patterns produced by each desmosomal antiserum in cryostat sections of a variety of tissues from a range of species

Anti-body	Skin						Heart						Liver						Gut					
	GP	B	H	R	C	F	GP	B	H	R	C	F	GP	B	H	R	C	F	GP	B*	H*	R	C	F
205/230	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+		+	+	+
150	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+		+	+	+
115	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+		+	+	+
100	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+		+	+	+
82/86	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+

Skeletal muscle and smooth muscle were negative with all antisera. Gut includes oesophagus, small intestine and stomach which gave similar patterns. GP = guinea pig, B = bovine, H = human, R = rat, C = chick, F = frog (*Rana pipiens*).

* Not done.

individual proteins each react with the other protein, so that the two proteins are immunologically very similar. (2) Antisera to D group glycoproteins reacted with these components only. (3) Anti-100K and anti-115K doublet each cross-reacted with the other glycoproteins in group C, in agreement with the monoclonal work of Cohen *et al.*⁷ (4) The anti-86K sera reacted with both the 86K and 82K proteins, suggesting their close relationship, although contamination has not been completely ruled out as an explanation for this result. Blotting experiments using whole tissue extracts of bovine nose, heart and liver showed that none of the antisera reacted with any other tissue components.

Ultrastructural studies have revealed that desmosomes of similar morphology are present in many tissues and their distribution is clearly circumscribed. Thus, in the mucosa of the stomach and intestine, desmosomes occur between the lateral

surfaces of the epithelial cells, usually as part of the junctional complex known as the terminal bar⁸. In the liver the apical regions of lateral surfaces of hepatocytes adjacent to bile canaliculi are linked by desmosomes⁹. In heart muscle, the adjacent muscle cells adhere at intercalated disks which are richly supplied with desmosomes¹⁰. Figure 2b-e shows staining of intestine, stomach, liver and heart, respectively. In each case the pattern of staining corresponded faithfully to the distribution of desmosomes known from ultrastructural studies. Staining was not observed elsewhere in the tissue. Furthermore, no staining of skeletal muscle (Fig. 2f) or chicken gizzard smooth muscle was obtained, indicating that the antibodies do not react with any of the muscle proteins which are associated with other junctions such as the zonula adherens¹¹. The antisera described by Franke *et al.*⁵ give similar staining patterns with bovine tissues. A brief report suggests that the monoclonal antibodies of Giudice *et al.*¹² show more limited cross-reactivity with bovine tissues, as would be expected from the nature of monoclonal antibodies.

Desmosomes occur in all vertebrate classes and wherever they occur their ultrastructure is similar¹³. It is possible, therefore, that their protein constituents are highly conserved and that antibodies against them would exhibit wide cross-reactivity between species. To test this, we have carried out fluorescent staining of the tissues of human, bovine, guinea pig, rat, chicken and frog. The results (Table 1) show that all our antibodies have wide cross-reactivity, although with certain clear exceptions. Thus, the skin of all species stains equally brightly with all five antibodies. Within the mammals all tissues stained with all antibodies. There was a reduction in staining intensity in heart, liver and gut with the anti-115K and anti-100K antibodies and this became more marked going down the evolutionary scale. Note that the titres of anti-100K and anti-115K determined by fluorescent staining of bovine nasal epithelium were equal to or greater than those of the other antibodies. Reduction in staining intensity might be explained by reduced cross-reactivity between tissue components, differences in penetration by the antibody due to different conformations in tissues or quantitative differences between antigens in different tissues. Frog heart stained with anti-86/82K only but other frog tissues stained with all five antisera, indicating that frog heart contains either 82K or 86K antigens, or both. (It is suspected that these antigens are immunologically distinct; M.S. Steinberg, personal communication.)

We conclude that desmosomes and desmosomal proteins are in general highly conserved. The fact that desmosomal antigens in different tissues are immunologically related does not necessarily mean that they show adhesive interaction. However, there is some evidence that their adhesive mechanisms interact between different vertebrate classes because mutual desmosomes form between reaggregated embryonic mouse and chick cells¹⁴. Taken together, these results support the view that molecular adhesive mechanisms are widely shared between different cell types.

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Developmental patterns of insulin-like growth factor-I and -II synthesis and regulation in rat fibroblasts

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Insulin-like growth factor-I (IGF-I) and IGF-II are chemically similar polypeptides with related receptor specificity and *in vitro* biological activity¹. IGF-I and IGF-II have a 62% amino acid sequence identity and are 38-48% homologous with the A and B domains of human proinsulin. They can be distinguished by specific radioimmunoassays, appear to have different patterns of hormonal regulation, and presumably serve different *in vivo* biological functions. Plasma IGF-II levels reflect circulating concentrations of pituitary growth hormone (GH), and exogenous IGF-I substitutes for GH in inducing somatic and skeletal growth in GH-deficient rats². Several recent observations in rats have suggested a possible role for IGF-II in fetal growth. IGF-II levels are 20- to 100-fold higher in fetal rat serum than in maternal serum and decline within days after birth³. IGF-I exhibits the reciprocal developmental pattern—low in the early neonate, rising to adult levels by approximately 4 weeks of age^{4,5}. We recently reported⁶ that cultured rat embryo fibroblasts synthesize large amounts of multiplication-stimulating activity (MSA or rIGF-II), the rat homologue of human IGF-II⁷. We now demonstrate that fibroblast cultures established from rats 2 to 50 days of age mimic the developmental switch from IGF-II to IGF-I production observed in serum. In addition, we show that placental lactogen (PL) but not GH stimulates IGF-II synthesis in fetal fibroblasts. By contrast, both GH and PL stimulate IGF-I synthesis in fibroblasts from older rats with no effect on IGF-II synthesis. Stimulation of IGF-II synthesis in fetal fibroblasts by PL provides a mechanism whereby PL may regulate fetal growth.

To determine whether the developmental pattern of IGF-I and IGF-II levels in blood was reflected in the IGF production pattern by fibroblasts derived from fetal and older rats, IGF-I and IGF-II concentrations were measured by specific radioimmunoassays in media conditioned by fibroblasts derived from skin and lung of rats of different ages (Fig. 1). The results of the MSA/rIGF-II and IGF-I/somatomedin-C (SM-C) radioimmunoassays are expressed as ng or µg equivalents of rIGF-II (M_r 8,700) and human IGF-I, respectively. The absolute values of IGF-II and IGF-I should not be compared, since rIGF-II (M_r 8,700) is 33% as potent as rIGF-III (M_r 7,100) in the MSA/rIGF-II radioimmunoassay⁸ and rIGF-I is 15% as potent as human IGF-I in the IGF-I/SM-C radioimmunoassay⁴. Thus, IGF-II levels are overestimated and IGF-I levels are underestimated. Levels of IGF-II were elevated in media from fetal fibroblasts and fibroblasts of younger pups (0.4 to 0.9 µg equivalents per 2×10^6 cells) and declined in media conditioned by fibroblasts from older animals. Fibroblasts derived from 11- to 21-day gestation whole embryos also synthesized IGF-II (0.5 to 1.0 µg equivalents per 2×10^6 cells per 48 h, data not shown). By contrast, the amount of IGF-I produced by fetal fibroblasts was low (<2.8 ng equivalents per 2×10^6 cells) and could be accounted for by rIGF-II cross-reacting in the IGF-I/SM-C radioimmunoassay¹³. However, fibroblasts from older animals secreted increased amounts of IGF-I (5 to 97 ng equivalents

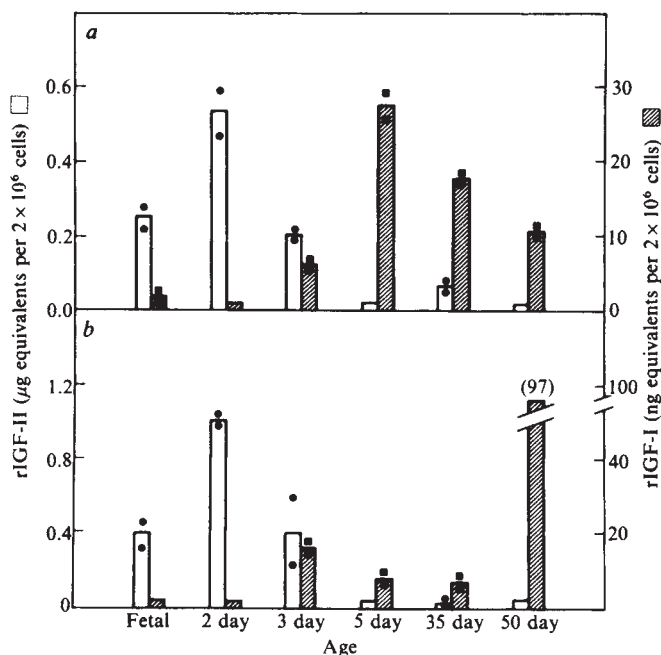


Fig. 1 Developmental pattern of IGF-I and IGF-II production by rat fibroblasts. Third passage fibroblasts, derived from lung (a) and skin (b) of embryos (16-day gestation) and rats of age 2, 3, 5, 35, and 50 days were plated in Temin's modified Eagle medium containing 0.25% fetal calf serum (2×10^6 cells per 60-mm dish)¹⁹. After cells attached, monolayers were washed and serum-free medium was added for a 24-h preincubation. Medium was discarded and 3 ml of serum-free medium was added. After 48 h medium was collected, centrifuged at 500g for 10 min and stored at -20°C . Experiments with fibroblasts derived from whole rat embryos showed that the level of IGF-II in the medium increased linearly from 3 to 72 h⁶. Conditioned medium was analysed in the MSA/rIGF-II (open bar) and IGF-I/SM-C (closed bar) radioimmunoassays^{3,6,20}. The MSA/rIGF-II radioimmunoassay used ¹²⁵I-rIGF-II (M_r 7,100)²¹, rabbit antiserum no. 422 which recognizes rIGF-II (M_r 8,700)²¹ and rIGF-II (M_r 7,100)⁸, and rIGF-II (M_r 8,700) as standard. Human IGF-I and a partially purified preparation of rIGF-I showed 4% and <0.05% cross-reactivity, respectively, in the MSA/rIGF-II radioimmunoassay⁸. The IGF-I/SM-C radioimmunoassay used purified IGF-I²², provided by René Humbel (Zurich, Switzerland) as radioligand and standard. The SM-C antiserum was provided by the hormone distribution program, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases. Rat IGF-I is 15% as reactive as human IGF-I in the IGF-I/SM-C radioimmunoassay⁴ and rIGF-II (MSA III-2, M_r 7,100) shows 1.2% cross-reactivity²³. Both assays were performed on duplicate dishes as previously described⁶. In order to validate the use of the radioimmunoassays performed directly on serum-free medium, 2-ml samples of medium were gel filtered on Sephadex G-50 in 1 M acetic acid to dissociate and separate IGF from binding protein. Levels of IGF in the medium were compared to levels in the post-void Sephadex G-50 pools in the MSA/rIGF-II and IGF-I/SM-C radioimmunoassays. In fetal fibroblast medium, IGF-II was $0.69 \mu\text{g ml}^{-1}$ in medium assayed directly and $0.65 \mu\text{g ml}^{-1}$ in the post-void Sephadex G-50 pool. In adult fibroblast medium, IGF-I was 7.5 ng ml^{-1} in medium assayed directly and 4.5 ng ml^{-1} in the Sephadex G-50 post-void pool. Thus the levels in a given sample were comparable before and after gel filtration.

per 2×10^6 cells (Fig. 1). The pattern of IGF-I production in fibroblasts from the older animals differed from lung and skin; IGF-I levels actually decreased after day 5 in lung fibroblasts.

The accumulation of IGF-II in fetal/neonatal fibroblast culture media, and of IGF-I in media incubated with older fibroblasts, appears to represent release of newly synthesized molecules. We previously demonstrated that cycloheximide reversibly inhibited IGF-II accumulation in medium condi-

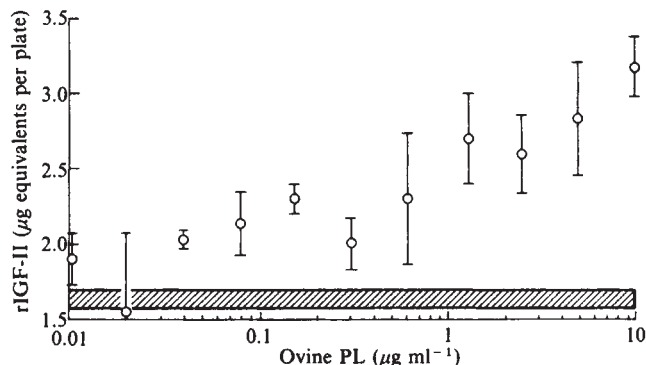


Fig. 2 Stimulation of IGF-II production in rat embryo fibroblasts by ovine PL. Third passage fibroblasts derived from 16-day rat embryos were preincubated in serum-free medium for 24 h and then fresh media containing different concentrations of ovine PL were added. Ovine PL was purified from term sheep cotyledons by ethanol homogenization, pH and ammonium sulphate precipitation, and gel and ion-exchange chromatography²⁴. The ovine PL was estimated to be purified to homogeneity (single band on acrylamide gel electrophoresis). After 48 h medium was collected from triplicate dishes and assayed in the MSA/rIGF-II radioimmunoassay. Rat IGF-II levels are expressed as μg per plate based on rIGF-II (M_r 8,700) standard. Cell number and total cellular protein were the same in dishes receiving medium alone or ovine PL. The vertical lines through the data points indicate ± 1 s.d. The hatched bar shows the IGF-II level in control cultures (± 1 s.d.). Significant stimulation (Student's *t*-test) was achieved at PL concentrations ($\mu\text{g ml}^{-1}$) of 0.04 ($P < 0.025$), 0.080 ($P < 0.025$), 0.16 ($P < 0.005$), 0.32 ($P < 0.05$), 0.62 ($P < 0.05$), 1.25 ($P < 0.005$), 2.5 ($P < 0.005$), 5.0 ($P < 0.001$), and 10 ($P < 0.001$).

tioned by fetal rat fibroblasts⁶. In older fibroblasts cycloheximide ($1 \mu\text{g ml}^{-1}$) caused a decrease in IGF-I from 22 to 43 ng equivalents per 2×10^6 cells to undetectable levels. We conclude that the developmental pattern of IGF-II and IGF-I synthesis by rat fibroblasts parallels the developmental profile in serum, providing evidence that fibroblasts in culture may be a suitable model for studying hormonal regulation of IGF production.

We next examined the ability of different hormones and growth factors to regulate IGF production in fibroblast cultures. At present, the hormonal control of fetal growth is poorly understood but appears not to involve GH^{9,10}. However, studies indicating that PL stimulated epiphyseal growth and IGF-I/SM-C production in immature GH-deficient rats suggest that PL may be important in regulating fetal growth^{11,12}. Rat embryo fibroblasts were incubated with ovine PL (0.01 to $10 \mu\text{g ml}^{-1}$) for 48 h and IGF-II in the medium was assayed by radioimmunoassay (Fig. 2). A twofold increase in IGF-II levels was observed at high concentrations of ovine PL; significant increase could be detected at 40 ng ml^{-1} ovine PL. Ovine PL appeared to increase IGF-II selectively, since there was a negligible effect on cell protein or number.

Stimulation of IGF-II levels in rat embryo fibroblasts was specific for ovine PL. Human GH (0.01 – $10 \mu\text{g ml}^{-1}$), insulin (0.01 – $10 \mu\text{g ml}^{-1}$), triiodothyronine (4 – 400 nM), dexamethasone (0.05 – $50 \mu\text{M}$), testosterone (4 – 400 ng ml^{-1}), oestradiol (2 – 200 ng ml^{-1}), epidermal growth factor (1 – 100 ng ml^{-1}), or platelet-derived growth factor (1 – $150 \text{ units ml}^{-1}$), caused no increase in rIGF-II in the medium after 54 h of culture (data not shown).

The increase in IGF-II accumulation in rat embryo fibroblast cultures incubated with ovine PL appeared to result from stimulation of IGF-II synthesis, rather than inhibition of IGF-II degradation. The amount of ³⁵S-cysteine incorporated into immunoprecipitable rIGF-II polypeptides (M_r 8,700 and 7,100) increased twofold when embryo fibroblasts were incubated with ovine PL (Fig. 3), suggesting that ovine PL stimulated the synthesis of IGF-II. The effect of ovine PL on IGF-II synthesis

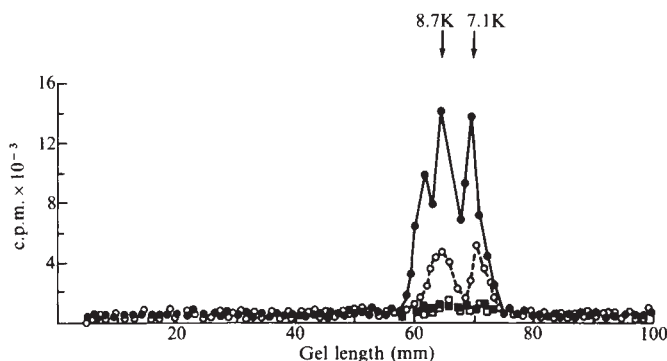


Fig. 3 Stimulation of ^{35}S -cysteine incorporation into rIGF-II polypeptides by ovine PL. Radioactivity (c.p.m.) is plotted against mobility (mm from the top) for immunoprecipitates from medium plus ovine PL (●); plus ovine PL, plus excess unlabelled rIGF-II (■); minus ovine PL (○); minus ovine PL, plus excess rIGF-II (□).

Methods: Third passage rat embryo fibroblasts, 2×10^6 cells per 60-mm plate, were preincubated in cysteine-free medium for 2 h, then 2 ml of medium with $200 \mu\text{Ci ml}^{-1}$ ^{35}S -cysteine (New England Nuclear) was added for 24 h with or without ovine PL ($3 \mu\text{g ml}^{-1}$). Medium was collected, lyophilized and desalted on a PD-10 column (Pharmacia) in 1 M acetic acid. The void volume was lyophilized and chromatographed on Sephadex G-50 in 1 M acetic acid. Post-void fractions corresponding to the elution volume of rIGF-II (M_r 8,700 and 7,100) standard were pooled, lyophilized and dissolved in 200 μl of borate-buffered saline with 0.5% bovine serum albumin. Immunoprecipitation was performed with 40 μl labelled material, 10 μl rIGF-II (M_r 8,700) antiserum no. 422 with or without 20 μg unlabelled rIGF-II (M_r 8,700) in a total volume of 80 μl . After overnight incubation at 4°C , 40 μl of 20% Pansorbin (Calbiochem) was added. After 1 h at 4°C , tubes were centrifuged for 4 min in a Beckman Microfuge and the supernatant was discarded. The pellet was washed four times with 500 μl buffer. The pellet was resuspended in 20 μl Laemmli buffer (0.125 M Tris-HCl, pH 6.8, 4% SDS, 10% glycerol), boiled for 3 min, and the supernatant was electrophoresed on a NaDodSO₄ 15% polyacrylamide slab gel²⁵. Rat IGF-II (M_r 8,700) and rIGF-II (M_r 7,100) were electrophoresed in parallel lanes. Lanes containing rIGF-II standards were fixed with 12% trichloroacetic acid in 25% methanol and stained with Coomassie blue. The lanes containing the immunoprecipitates were frozen and immediately sliced in 1-mm sections. Gel slices were placed in scintillation vials with 3% Protosol (New England Nuclear), toluene and Liquafluor (New England Nuclear). After 24 h at 37°C , radioactivity in the vials was measured. The radioactivity in the immunoprecipitates was not increased by doubling the amount of antiserum. Total trichloroacetic acid-precipitable radioactivity was the same in medium from both the control and the ovine PL-stimulated cultures (112,370 c.p.m. versus 112,980 c.p.m.). Immunoprecipitation was also performed with antiserum no. 2, specific for rIGF-II (M_r 8,700), and immunoprecipitates analysed in an acid-urea gel electrophoresis system²¹. The mobility of the immunoprecipitates (c.p.m.) coincided with the position of rIGF-II (M_r 8,700) standard, and ovine PL caused a 2.6-fold increase in radioactivity (18,366 c.p.m. versus 7,100 c.p.m.).

was selective since PL did not cause an increase in ^{35}S -cysteine incorporation into total trichloroacetic acid-precipitable material. To determine whether ovine PL was increasing IGF-II levels by affecting degradation, rat embryo fibroblasts were incubated in serum-free medium with or without ovine PL for 48 h, followed by addition of cycloheximide to inhibit protein synthesis. After the addition of cycloheximide, the amount of IGF-II remained constant for 48 h (data not shown), indicating that ovine PL was not influencing the rate of degradation of IGF-II.

We next examined the regulation of IGF-I and IGF-II synthesis in adult rat lung fibroblasts (Fig. 4). Levels of IGF-I and IGF-II in conditioned medium of adult rat lung fibroblasts cultured in the presence of hGH or ovine PL were determined by radioimmunoassay. Growth hormone has been shown to increase the amount of IGF-I/SM-C produced by human skin

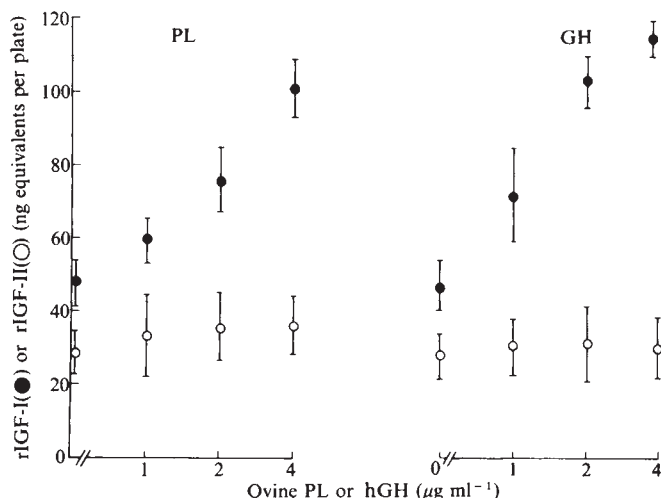


Fig. 4 Stimulation of IGF-I production in adult rat fibroblasts cultured with ovine PL or hGH. Adult (25 days) rat lung fibroblasts in serum-free medium were incubated for 48 h with hGH provided by the hormone distribution program, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, or ovine PL, purified as described in Fig. 2. Levels of IGF-II (○) and IGF-I (●) were measured by radioimmunoassay on media from triplicate dishes as described in Fig. 1. The vertical line indicates ± 1 s.d.

and lung fibroblasts^{13,14}. Both hGH ($1\text{--}4 \mu\text{g ml}^{-1}$) and ovine PL ($1\text{--}4 \mu\text{g ml}^{-1}$) increased the amount of IGF-I in medium from adult fibroblasts. By contrast, the levels of IGF-II, which were much lower than in medium from fetal fibroblasts, were not increased by addition of ovine PL or hGH. Ovine PL has been shown to increase blood IGF-I/SM-C levels in GH-deficient rats¹², presumably by interaction with the GH receptor^{15,16}; ovine PL may be stimulating IGF-I/SM-C production in adult fibroblasts by a similar mechanism. By contrast, in fetal fibroblasts ovine PL, but not hGH, stimulates IGF-II synthesis, suggesting that ovine PL may be acting through a receptor other than the GH receptor in fetal tissue. A distinct ovine PL receptor is also suggested by the finding that ovine PL, but not hGH, increased ornithine decarboxylase activity (ODC) in fetal rat livers while both ovine PL and hGH increased ODC activity in adult livers¹⁷.

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Control of timing of cell cycle events in fission yeast by the *wee 1*⁺ gene

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The means by which cells control the timing of events in the cell division cycle have been investigated in depth recently. The existence of controls over the major events of DNA replication and mitosis has been demonstrated in several systems; controls of both events have been identified in the yeasts *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*. The control points have been defined on the basis of cell cycle arrest caused by certain mutations¹⁻⁴ or mating pheromones⁵, and by growth-related parameters^{3,6-10}. Investigation of how the component processes, generally identified by specific genes, are organized into developmental pathways^{11,12} has provided much information on how the proper temporal order of events is maintained, but little is known about the control of the absolute timing of the component processes in the cycle. The time of completion of a gene-controlled process in the cell cycle can be estimated from the transition or execution point of a temperature-sensitive mutant defective in the particular gene¹³. In the fission yeast *S. pombe* the transition points of most mutants defective for mitosis are temporally clustered shortly before the event¹⁴, but the mechanism which maintains this coordination has not been investigated. I report here that the transition points of three genes required for mitosis are advanced in strains carrying a *wee 1* mutation, whose best known effect is to reduce cell size at mitosis¹⁵. The observed advancement can be as much as 0.4 of the cycle, implicating the *wee 1*⁺ gene in a system which controls the timing and temporal coordination of developmental steps controlled by three mitotic genes.

Cultures of various strains carrying different temperature-sensitive mutations preventing the completion of mitosis were shifted from exponential growth at the permissive temperature to the restrictive temperature. The pattern of cell division was followed by determining the cell number per ml of culture (see Fig. 1). From these and similar experiments the fractional increase in cell number after shift was calculated for each strain (Table 1). All the mutants tested showed a residual increase in number of about 25%, with the exception of *cdc 6.23*, which showed an incomplete arrest with a residual increase of ~54%. A wild-type culture treated with the antimitotic agent benomyl¹² at 25 °C showed a similar pattern of division, with an increase in cell number of 28%.

In the conditions used, mitosis in *S. pombe* occurs between 0.75 and 0.8 through the cell cycle. The characteristic increase in cell number of 25% corresponds to a transition point for the mutants of ~0.68 in the cell cycle¹⁴. Thus, several processes controlled by cell cycle genes which are required for mitosis are completed shortly before mitosis itself, as previously noted¹⁴.

Double mutants carrying a conditional mitotic mutation and a cell size mutation were constructed. The single mutant strains used were all originally derived from the wild-type 972h⁻ by mutation, followed by at least one backcross to the isogenic

wild-type 975h⁺ (ref. 16). The differences between *wee 1*⁻ and *wee 1*⁺ strains described below are therefore probably due to this single gene difference.

Cultures of the various single and double mutants were shifted from the permissive to restrictive temperature. In each case, including the *wee 1*⁻ *cdc*⁻ double mutants, the cell cycle defect was expressed, and cells were unable to divide at the restrictive temperature, in contrast to the behaviour of *wee 1*⁻ *cdc 25*⁻ double mutants¹⁷. However, the presence of a *wee 1* mutation in some cases had a dramatic effect on the fraction of cells able to divide after the shift (Fig. 1, Table 1). Specifically, *cdc 1*⁻ and *cdc 27*⁻ strains carrying a *wee 1* mutation showed a much greater increase in cell number than the parent *cdc*⁻ strains. The effect seemed to be gene- rather than allele-specific, as the presence of *wee 1.1*, *wee 1.3* or *wee 1.6* gave rise to very similar effects in the *cdc* strains tested. Furthermore, both *cdc 1* mutations behaved in a similar way in the presence of *wee 1.6* (Table 1).

One possible explanation of the phenomenon was that in certain *wee 1*⁻ *cdc*⁻ double mutants, mitosis occurred much earlier than usual relative to cell division. If this were the case, then the *cdc* gene product might complete its function shortly before mitosis, just as in *wee*⁺ strains, but a substantially greater fraction of cells would divide after temperature shift. This explanation can be excluded, as the fraction of binucleate cells in *wee 1*⁻ strains during growth at 25 °C was very similar to that in the corresponding *wee 1*⁺ strains. The percentage of binucleate cells was 18.5% for *wee 1*⁻ *cdc 1.7* compared with 14.3% for *wee 1*⁺ *cdc 1.7*; and 20.8% for *wee 1*⁻ *cdc 2.33* compared with 14.9% for *wee 1*⁺ *cdc 2.33* (mean values of at least two independent experiments for each strain). Mitosis therefore occurs at a similar stage of the cell cycle, about three-quarters of the way through, in all these strains.

Double mutants of *cdc 1.7* with *wee* alleles of *cdc 2* (*cdc 2-w* alleles, formerly *wee 2*; see ref. 3) did not show an increased fraction of cells dividing after shift to the restrictive temperature (Fig. 1, Table 1). It is therefore unlikely that reduced cell size at 25 °C itself causes the changed division pattern, as *cdc 2-w*

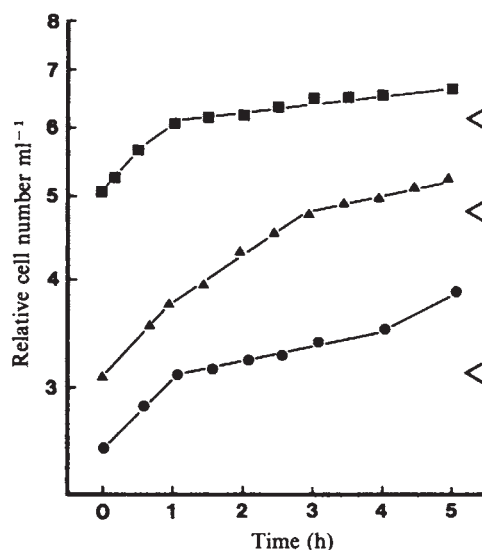


Fig. 1 Effect of temperature shift on *cdc 1* strains. Exponential cultures of *cdc 1.7* (■), *wee 1.6 cdc 1.7* (▲) and *cdc 2.1w cdc 1.7* (●) were grown at 25 °C in minimal medium EMM 2 as modified by Nurse¹⁹. At time zero, portions were shifted to 36 °C and sampled at intervals for cell number ml⁻¹ estimation. The results are plotted on a semi-logarithmic scale, with 1 unit of the ordinate equivalent to 10⁶ (*cdc 1.7*), 2 × 10⁶ (*wee 1.6 cdc 1.7*) and 0.5 × 10⁶ (*cdc 2.1w cdc 1.7*) cells per ml of culture. As all three strains showed slightly incomplete arrest at 36 °C, the fraction of cells able to divide after shift was estimated from the first time at which the rate of cell number increase fell to a much lower value. The cell number level used for calculation is indicated by the large open triangles.

Table 1 Transition points of *cdc* and *cdc wee* mutant strains

<i>cdc</i>	<i>wee</i> ⁺	<i>wee</i> 1.1	<i>wee</i> 1.3	<i>wee</i> 1.6	<i>cdc</i> 2-1w	<i>cdc</i> 2-2w
1.7	1.27 ± 0.05 (0.65)	1.58 (0.34)	1.56 (0.35)	1.63 ± 0.05 (0.29)	1.28 ± 0.07 (0.64)	1.34 (0.58)
1.P13	1.30 (0.62)			1.59 (0.33)		
2.33	1.24 ± 0.03 (0.69)	1.42 (0.49)	1.44 (0.47)	1.43 ± 0.05 (0.48)		
2.L7	1.25 (0.68)			1.44 (0.47)		
2.M26	1.27 (0.65)			1.38 (0.53)		
2.M55	1.27 (0.65)			1.42 (0.49)		
2.M63	1.23 (0.70)	1.19 (0.74)	1.20 (0.73)	1.25 (0.68)		
2.M35	1.26 (0.66)			1.19 (0.74)		
6.23	1.54 (0.37)			1.67 (0.26)		
13.117	1.24 (0.69)			1.16 (0.78)		
27.K3	1.30 (0.62)			1.71 (0.22)		
<i>ben</i> 4.D19	1.18 (0.75)			1.17 (0.77)		
Benomyl	1.20 (0.73)			1.27 (0.65)		

The table shows the ratio of final to initial cell number ml⁻¹ after shifting a culture¹⁴ in minimal medium¹⁹ from permissive to restrictive temperature. The first value shown is the fractional increase, with standard deviations given where at least five independent cultures were tested. The second value (in parentheses) is the transition point expressed as a fraction of the cell cycle, calculated as described in ref. 14. Details of the strains are given in refs 14, 16 and 20; *ben* 4.D19 is described elsewhere²¹. Permissive and restrictive temperatures of 25 °C and 35–36 °C were used, except for the cold-sensitive mutation *ben* 4.D19 where 35 °C (permissive) and 20 °C (restrictive) were used. The effect of benomyl (20 µg ml⁻¹) was tested on 972 *h*⁻ and *wee* 1.6 *h*⁻ cells growing at 25 °C.

cdc 1.7 cells are closer in size to *wee* 1⁻ *cdc* 1.7 than to *wee*⁺ *cdc* 1.7 cells (Table 2).

In contrast to the behaviour of *cdc* 1⁻ and *cdc* 27⁻ strains, double mutants of *cdc* 13⁻ or *ben* 4⁻ with *wee* 1⁻ behaved after shift in a very similar way to the parent *cdc*⁻ or *ben*⁻ mutants (Table 1). Strains *cdc* 6.23 and *wee* 1.6 *cdc* 6.23 showed incomplete division arrest, making a precise estimate of the fraction of cells dividing impossible. The increase in dividing fraction from ~54% to ~67% may not be significant. The action of benomyl on *wee* 1.6 cells was very similar to that on the wild type (Table 1).

The effect of a *wee* 1⁻ mutation on *cdc* 2 mutants depended on the *cdc* 2⁻ allele concerned. With *cdc* 2.M35 and *cdc* 2.M63 the fraction of cells dividing was unaffected by the presence of *wee* 1 mutations, while the other four *cdc* 2⁻ mutants tested did show altered behaviour (Table 1). The increase in dividing fraction was from ~25% to 40%, a smaller effect than for *cdc* 1⁻ or *cdc* 27⁻, but nevertheless highly repeatable (note the small standard deviations for *cdc* 2.33 and *wee* 1.6 *cdc* 2.33 in Table 1). In those cases tested the behaviour was independent of the mutant *wee* 1 allele: *cdc* 2.33 showed a consistent change in the presence of any of three *wee* 1 alleles, while *cdc* 2.M63 showed no change in any double mutant (Table 1).

The presence of a *wee* 1 mutation in *S. pombe* strains carrying a temperature-sensitive mutation in three genes required for mitosis increases the fraction of cells able to undergo mitosis and cell division following a shift from permissive to restrictive temperature. This can be explained by the proposal that *wee* 1⁻ cells complete the particular developmental steps controlled by the *cdc* genes earlier in the cycle than do *wee* 1⁺ cells. In the case of *cdc* 1, the function of its product is completed at 25 °C by the transition point in the cycle of 0.65 (Table 1). On shifting an asynchronous culture from 25 °C to 35 °C the 27% of cells

that are past the transition point are able to divide. In the double mutant *wee* 1.6 *cdc* 1.7, 63% of the cells divide after shift, corresponding to a transition point of 0.29, suggesting that the *cdc* 1 function is complete at this time. Similar arguments apply to *cdc* 2⁻ and *cdc* 27⁻ strains. One explanation is that a function of the wild-type *wee* 1⁺ gene product is to inhibit the activities of the products of *cdc* 1⁺, *cdc* 2⁺ and *cdc* 27⁺. The extent of this inhibition would not be total: rather, the degree of inhibition would delay completion of the processes controlled by the various *cdc* genes until an appropriate stage in the cycle. In *wee* 1⁻ mutants the inhibition would be relieved, the processes controlled by the *cdc* genes would therefore proceed faster and be complete at an earlier stage in the cycle.

It has been suggested that both the *wee* 1⁺ and *cdc* 2⁺ genes are concerned with rate-limiting processes leading to entry into mitosis³. According to the proposal made here, the *wee* 1⁺ product inhibits the *cdc* 2⁺-controlled process required for mitosis; relief of the inhibition in a *wee* 1⁻ mutant allows the process to be completed earlier in the cycle. The advancement of transition point of some *cdc* 2⁻ mutants relative to mitosis suggests that in *wee* 1⁻ strains some process other than that controlled by *cdc* 2⁺ is rate-limiting for mitosis. The existence of a second pathway controlling entry into mitosis in *wee* strains was proposed earlier on the basis of different evidence¹⁸. In support of the idea is the observation that the two *cdc* 2 alleles whose transition points are not affected in *wee* 1⁻ strains cause a substantial increase in cell size at 25 °C (Table 2). The increased size compared to *cdc* 2⁺ cells is apparent in *wee* 1⁻ strains (Table 2; ref. 3) and to a lesser extent in *wee* 1⁻ strains (Table 2). If the mutant products of *cdc* 2.M35 and *cdc* 2.M63 showed reduced activity at 25 °C, this would account for the increased cell size in *wee* 1⁺ strains. In addition, the process controlled by *cdc* 2 would occur at a lower rate in *wee* 1⁻ as well as in *wee*⁺ cells, and therefore might still be rate-limiting for entry into mitosis in the *wee* 1⁻ strains. This is consistent with the increased cell size of *wee* 1⁻ *cdc* 2.M35 and *wee* 1⁻ *cdc* 2.M63 double mutants and with the late transition points of the *cdc* 2 mutations in the double mutant strains.

Loss of *wee* 1⁺ function causes advancement of the transition points of *cdc* 1, *cdc* 27 and some *cdc* 2 alleles, but to different extents (Table 1). In contrast, the transition points in *wee* 1⁺ strains are close together in time. The normal temporal coordination could be brought about by a balance between the activity of each *cdc* gene product and inhibition of the activity by the *wee* 1⁺ gene product. The degree of inhibition might differ for the various *cdc* gene products, and loss of inhibitory activity in *wee* 1⁻ strains would then differentially affect the times of completion of the *cdc* gene-controlled processes. Other processes, such as those controlled by *cdc* 13, *ben* 4 and perhaps

Table 2 Cell lengths at division of *cdc* and *wee cdc* strains

<i>cdc</i>	<i>wee</i> ⁺	<i>wee</i> 1	<i>cdc</i> 2.1w	<i>cdc</i> 2.2w
+	12.8	8.2	9.2	8.6
1.7	14.9	8.4	9.5	9.7
2.33	14.2	8.9		
2.L7	14.6	8.5		
2.M26	13.2	8.9		
2.M55	14.4	8.7		
2.M63	16.7	9.6		
2.M35	22.4	10.3		

Cultures were grown at 25 °C and samples were taken to estimate cell length (in µm) of cells with septa, that is, shortly before cell separation. At least 24 cells were measured per culture. Some data from ref. 3 were included.

cdc 6, seem not to be under *wee 1* control, and can perhaps occur only after completion of other (unknown) events.

Previous studies^{3,12} have suggested the rate-limiting nature of the *cdc 2* step and several other events seem dependent on its completion, in particular the *cdc 1* step. However, in *wee 1*⁻ cells the *cdc 1* step is apparently completed before the *cdc 2* step (Table 1), implying an effect which precedes its cause. One possible explanation of this is that loss of *wee 1*⁺ function uncouples normal dependency relationships.

The proposed inhibition of the activity of several *cdc* gene-controlled developmental steps might be mediated in several ways. The *wee 1*⁺ product might repress expression of several

cdc genes, implying that the expression of *cdc* genes is important in determining the time of action of the corresponding gene product (see ref. 12). Alternatively, the inhibition might operate at the level of protein-protein interactions, perhaps between the *wee 1*⁺ and *cdc*⁺ gene products themselves. These possibilities can only be resolved by identification and analysis of the various gene products.

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Measurement of *in vivo* mutations in human lymphocytes

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A means of measuring *in vivo* mutations in man would be valuable in assessing the importance of mutation in ageing and human disease and for monitoring individuals exposed to environmental mutagens and carcinogens. The hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus has been used to study mutagenesis in cultured mammalian (and other) cells¹; clones are selected by their ability to grow in the presence of the purine analogue, 6-thioguanine (6-TG). Such clones are almost always HGPRT⁻ and are therefore probably the progeny of a mutant cell. This system has been applied to human lymphocytes by using autoradiography to detect single mutant cells²⁻⁶. This approach probably does detect mutant cells, particularly if their number is increased, but the results obtained are variable and rather imprecise^{4,5}. Also, the technique does not allow isolation of clones, thus the mutational origin of thioguanine-resistant (TG^r) cells cannot be determined as the gene product, HGPRT, cannot be measured. Previous methods for cloning peripheral blood lymphocytes (PBL) have been so inefficient that detection of TG^r lymphocytes has not been practicable. We have cloned PBL by a technique which is highly efficient (20-60% of PBL form a clone) and results in large clones of 10³-10⁴ cells that are readily scored using an inverted microscope^{6,7}. We report here that the *in vivo* mutation frequency is of the order of that observed for human fibroblast lines cultured *in vitro*¹.

The use of 6-TG as a selection agent is based on the use of a concentration of 6-TG on the plateau of the dose-response curve. At this concentration, TG^r clones represent a qualitatively different, presumably mutant population, rather than rare clones at the extremes of the gaussian distribution of the wild-type population. Using the limiting dilution technique^{7,8}, 6-TG dose-response curves were obtained in two individuals by measuring the proportion of clones able to grow at varying 6-TG concentrations; the results (see Fig. 1) indicate a plateau

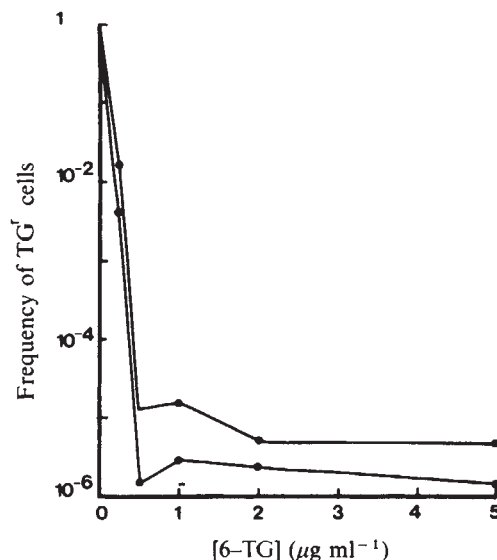


Fig. 1 Thioguanine dose-response curves for two individuals. Lymphocytes were separated by Ficoll-Hypaque centrifugation, washed and cultured in microwells in 0.2 ml of modified McCoy's medium containing phytohaemagglutinin (PHA, Wellcome reagent grade, 2.5 μl ml⁻¹) and 10% conditioned medium as a source of interleukin-2. The conditioned medium had been prepared by culturing PHA-stimulated, irradiated mixed tonsillar lymphocytes for 48 h (ref. 7). In addition to target lymphocytes, each well contained 10⁴ autologous lymphocytes irradiated with 5,000 rad. Wells without 6-TG contained doubling dilutions of from 10 to 0.625 cells per well whereas wells with 6-TG contained 10⁴ or 10³ cells per well. Plates were read after 16 days of culture, the cloning efficiencies with and without 6-TG were calculated from the proportion of negative wells⁸, and the frequency of TG^r clones calculated as the ratio of the cloning efficiencies.

of survival above a 6-TG concentration of 0.5 μg ml⁻¹. Other data from two hemizygotes and three heterozygotes for the naturally occurring mutation, Lesch-Nyhan (L-N) syndrome, showed a similar plateau. Based on these findings, all further 6-TG selection studies used a concentration of 2.5 μg ml⁻¹ and 96 microwells containing 10⁴ target lymphocytes per well. To date, 14 normal individuals of both sexes, aged 23-44, have

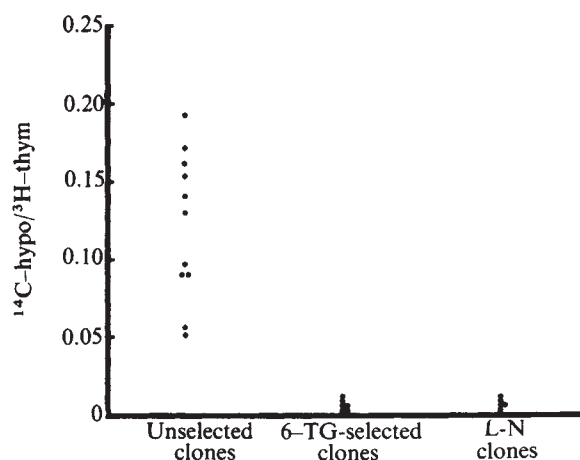


Fig. 2 Hypoxanthine incorporation in clones from one experiment. Clones were washed three times in the microplates and pulsed overnight with $0.05 \mu\text{Ci}$ of ^{14}C -hypoxanthine (^{14}C -hypo) and $0.25 \mu\text{Ci}$ ^3H -thymidine (^3H -thym). The cells were collected onto glass fibre disks which were washed and counted. Selected and unselected clones were isolated from the same individual.

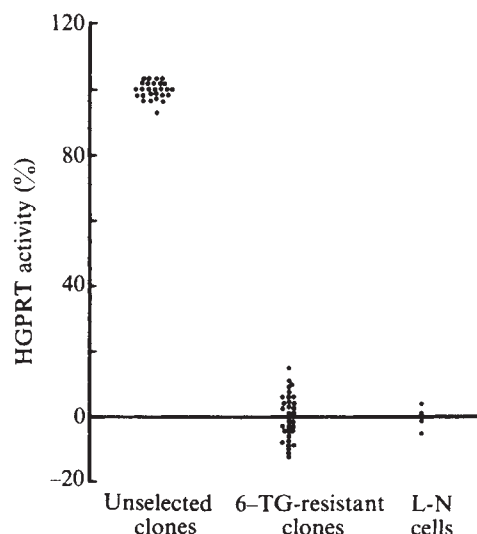


Fig. 3 HGPRT assays in 6-TG-selected and unselected clones from two individuals. Clones were expanded for 10–14 days by adding PHA plus 5×10^5 irradiated feeder lymphocytes to each clone and then refeeding at 3–4-day intervals with medium containing interleukin-2. After expansion the cells were washed, the concentration adjusted to 10^7 ml^{-1} and aliquots frozen at -70°C until assay. The results shown are the mean of duplicate assays.

been studied. The geometric mean for the frequency of TG^r cells was 3.0×10^{-6} with the 95% confidence limits (mean $\pm$ 2 s.d.) of 1.6×10^{-5} – 5.4×10^{-7} .

To obtain further evidence that the 6-TG-selected clones were mutants, we measured ^{14}C -hypoxanthine incorporation into individual clones and directly measured HGPRT activity in individual clones. As different clones contained different numbers of cells, ^{14}C -hypoxanthine incorporation was measured as the ratio of ^{14}C -hypoxanthine to ^3H -thymidine incorporation into individual clones. The results (Fig. 2) indicate that hypoxanthine incorporation was low in all TG^r clones compared with that observed for unselected clones, and was similar to that observed for unselected clones from a hemizygote with L-N syndrome. For measurement of HGPRT activity, unselected and 6-TG-selected clones were expanded by adding irradiated feeder lymphocytes to each clone and growing them for 10–14 days in 6-TG-free medium containing interleukin-2. HGPRT activity was then assayed by measuring the conversion of ^3H -hypoxanthine to ^3H -IMP (measured as ^3H -IMP + ^3H -inosine)⁹. In one experiment the mean conversion of hypoxanthine by unselected clones was 98% and in the other it was 60%; the results for both experiments were normalized so that the HGPRT activity for each clone assayed was expressed as a percentage of the mean for the unselected clones in that experiment. The results (Fig. 3) indicate that TG^r clones converted little or no hypoxanthine compared with unselected clones. Uncloned L-N lymphocytes, included as negative controls, similarly converted little or no hypoxanthine. In the assay conditions, ^3H -hypoxanthine conversion was linearly related to HGPRT level and the results therefore indicate that the TG^r clones had little or no HGPRT activity.

The results therefore show that rare TG^r lymphocytes are present in the blood of normal individuals: the 6-TG resistance of clones derived from the lymphocytes, their inability to incorporate hypoxanthine and the lack of HGPRT in the clones, all suggest that these circulating TG^r lymphocytes represent naturally occurring mutations. The genetic basis for the mutations remains to be investigated but is of obvious interest.

Our estimate for *in vivo* mutation frequency is of the order of that observed for human fibroblast lines cultured *in vitro*¹. However, it might be argued that our data underestimate the

true *in vivo* mutation frequency due to several factors. Metabolic cooperation between mutant and non-mutant cells could conceivably lead to killing of mutant cells but other results from our laboratory, involving co-culture of L-N and normal cells, have shown no evidence of this phenomenon. The selection conditions of the present assay, as evidenced by the data in Fig. 1, were deliberately chosen to be highly stringent and it is likely that missense mutants having some functional HGPRT were not detected. Indirect evidence from the autoradiographic technique suggests that mutants having some HGPRT might be three to four times as common as mutants lacking HGPRT⁵ but it should now be possible to investigate this problem directly by using clonal analysis and less stringent selection conditions such as use of azaguanine or a lower concentration of 6-TG.

In addition to allowing measurement of mutation frequency *in vivo*, the present technique can also be used for continuously cultured lymphocytes⁷. We should be able to measure pre-mutational lesions *in vivo* by allowing a period for expression in culture before measuring mutations. By exposing lymphocytes to a defined mutagenic stimulus, allowing time for expression and then measuring induced mutations, the process of mutagenesis could be studied both in normal human cells and in cells from individuals of particular interest.

Since submission of this manuscript, another paper¹⁰ reporting isolation of TG^r lymphocyte clones has been published.

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The gene encoding the Ia antigen-associated invariant chain (I_i) is not linked to the $H-2$ complex

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The invariant (I_i) chain of murine Ia antigens is associated with the intracellular but not the cell-surface forms of the $A_\alpha:A_\beta$ and $E_\alpha:E_\beta$ Ia complexes¹⁻³. Due to its unique subcellular localization, I_i has been postulated to play a part in the assembly⁴ or intracellular transport⁵ of the Ia $\alpha:\beta$ complexes, which function in immune recognition⁵⁻⁷. A more general role for I_i in the transport of other cell proteins has also been suggested⁸. Because of the unusual subunit composition of Ia antigens and because the synthesis of α , β and I_i chains is coordinately regulated⁹, it was of interest to determine whether, like the α and β chains¹⁰⁻¹², I_i is encoded by a gene in the I region of the $H-2$ histocompatibility complex. We report here the use of an I_i chain polymorphism present in *Mus spretus*¹³ to demonstrate that the gene for I_i is not linked to the $H-2$ complex. Thus, intracellular Ia antigens consist of the products of two linked genes and one unlinked gene.

Efforts to determine possible linkage of the gene encoding I_i to the $H-2$ complex have been hampered by the absence of detectable polymorphism in I_i among inbred mouse strains. To find an electrophoretic variant of I_i which could be used for mapping studies, we screened by two-dimensional polyacrylamide gel electrophoresis (PAGE) spleen cell extracts from wild-derived mouse stocks (developed by Dr Richard Sage of the University of California, Berkeley). Fifty mice, spanning 15 different species and subspecies of the genus *Mus*, were included in the study. Although several species had I_i chains which could be distinguished electrophoretically from that of laboratory mice¹³, only one, *M. spretus*, was a house mouse within the subgenus *Mus* and thus likely to produce viable,

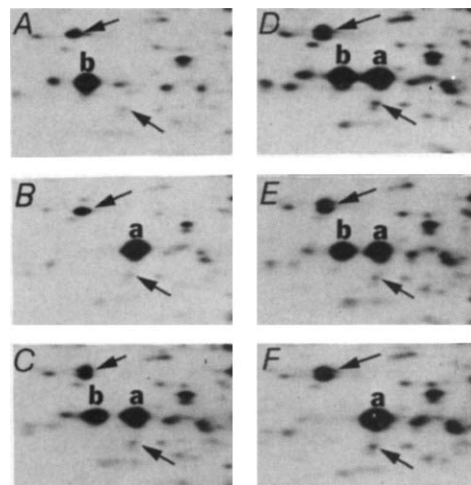


Fig. 1 Determination of the I_i genotype. Extracts of ³⁵S-methionine-labelled spleen cells were prepared and analysed by two-dimensional PAGE as described by Jones¹⁷. Molecular weight decreases from top to bottom. The more acidic proteins are to the right and the more basic proteins are to the left. Portions of the fluorograms containing the I_i chain are shown, including basic proteins with molecular weights in the approximate range of 25,000–35,000. The spot marked by the letter a corresponds to the I_i^a chain; the spot marked by the letter b corresponds to the I_i^b chain. The arrows indicate two reference spots which aid in comparison of the positions of the I_i chains. A, *M. spretus*; B, BALB/c; C, mixture of *M. spretus* and BALB/c; D, (BALB/c $\times$ *M. spretus*) F₁ δ 8731; E, backcross mouse 9350; F, backcross mouse 9346.

fertile progeny in crosses with laboratory mice. F₁ and backcross mice produced in crosses between *M. spretus* and BALB/c were used for a conventional linkage study.

M. spretus males derived from mice trapped by Sage in Cadiz, Spain, were crossed with BALB/c females. Both male and female F₁ hybrids were obtained but only the females seem to be fertile. Thus, all backcross progeny were offspring of the cross (BALB/c $\times$ *M. spretus*) F₁ δ $\times$ BALB/c δ . The backcross mice used for the linkage analysis came from four litters

Fig. 2 Confirmation that *M. spretus* has a variant form of the I_i chain. ³⁵S-methionine labelling of spleen cells, immunoprecipitations and two-dimensional PAGE were as described by Jones¹⁷. The spot marked by the letter a corresponds to the I_i^a chain; the spot marked by the letter b corresponds to the I_i^b chain. A_α and A_β are the component Ia chains; the superscripts refer to the haplotype origins of the polypeptides, d for the BALB/c-derived chains and sp for the *M. spretus*-derived chains. A, A representative control gel showing results of immunoprecipitation of *M. spretus* extract with the anti- $I-A^d$ monoclonal antibody, MK-D6 (a gift from Drs P. Marrack and J. Kappler of the University of Colorado Medical School). B, *M. spretus* extract with the anti- $I-A^k$ monoclonal antibody 10-3.6 (ref. 18). C, BALB/c ($I-A^d$) extract with MK-D6. D, (BALB/c $\times$ *M. spretus*) F₁ 5502 extract with 10-3.6. E, extract from backcross mouse S1 with MK-D6. F, extract from backcross mouse S3 with MK-D6. The *M. spretus* A_β protein is to the left of I_i , and not included in the area of the gel shown. The monoclonal antibody 10-3.6 recognizes a determinant on A_β^d . A_β^d is not recognized by 10-3.6 and thus is not immunoprecipitated from the F₁ extract (panel D). A_α^d and A_α^{sp} are both immunoprecipitated from the F₁, thus demonstrating that both allelic forms of A_α can associate with A_β^d .

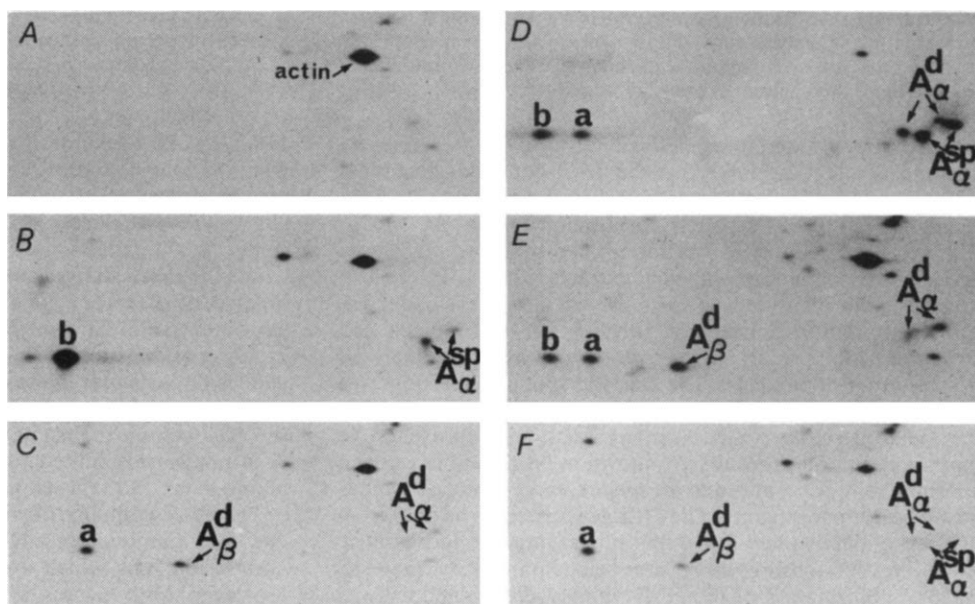


Table 1 Linkage analysis of *Ii*

Mouse‡	Monoclonal antibody reactivity*			Summary of results†				
	MK-D6	10-3.6	3JP	H-2§	<i>Ii</i>	β_2m #	Albino**	
BALB/c	+	—	—	<i>d/d</i>	<i>a/a</i>	<i>a/a</i>	<i>c/c</i>	
<i>M. spretus</i>	—	+	+	<i>sp/sp</i>	<i>b/b</i>	<i>sp/sp</i>	<i>c⁺/c⁺</i>	
F ₁ 8731	+	—	+	<i>sp/d</i>	<i>b/a</i>	<i>sp/a</i>	<i>c⁺/c</i>	
F ₁ 7919	+	+	+	<i>sp/d</i>	<i>b/a</i>	<i>sp/a</i>	<i>c⁺/c</i>	
BC S1	+	—	—	<i>d/d</i>	<i>b/a</i>	<i>sp/a</i>	<i>c/c</i>	
BC S2	+	+	+	<i>sp/d</i>	<i>a/a</i>	<i>a/a</i>	<i>c⁺/c</i>	
BC S3	+	+	+	<i>sp/d</i>	<i>a/a</i>	<i>sp/a</i>	<i>c/c</i>	
BC S4	+	—	—	<i>d/d</i>	<i>b/a</i>	<i>sp/a</i>	<i>c⁺/c</i>	
BC S5	+	—	—	<i>d/d</i>	<i>b/a</i>	<i>a/a</i>	<i>c⁺/c</i>	
BC S6	+	+	+	<i>sp/d</i>	<i>a/a</i>	<i>sp/a</i>	<i>c⁺/c</i>	
BC S7	+	+	+	<i>sp/d</i>	<i>a/a</i>	<i>sp/a</i>	<i>c⁺/c</i>	
BC 9346	+	—	—	<i>d/d</i>	<i>a/a</i>	<i>sp/a</i>	<i>c⁺/c</i>	
BC 9347	+	—	—	<i>d/d</i>	<i>a/a</i>	<i>a/a</i>	<i>c⁺/c</i>	
BC 9348	+	—	—	<i>d/d</i>	<i>a/a</i>	<i>sp/a</i>	<i>c/c</i>	
BC 9349	+	—	+	<i>sp/d</i>	<i>a/a</i>	<i>a/a</i>	<i>c/c</i>	
BC 9350	+	—	—	<i>d/d</i>	<i>b/a</i>	<i>a/a</i>	<i>c⁺/c</i>	

* The determination of monoclonal antibody reactivity was done as shown in Fig. 3.

† If *H-2* and *Ii* were tightly linked, only backcross progeny with the genotypes *H-2^d/H-2^d*, *I^a_i/I^a_i* and *H-2^{sp}/H-2^d*, *I^b_i/I^a_i* would be expected. If β_2m and *Ii* were tightly linked only backcross progeny with the genotypes β_2m^a/β_2m^a , *I^a_i/I^a_i* and β_2m^{sp}/β_2m^a , *I^b_i/I^a_i* would be expected. If albino (*c*) and *Ii* were tightly linked, only backcross progeny with the genotypes *c/c*, *I^a_i/I^a_i*, and *c⁺/c*, *I^b_i/I^a_i* would be expected.

‡ All *M. spretus* mice tested so far exhibit the antibody reactivities and the *Ii*, β_2m and albino genotypes indicated on the second line. Both F₁ 8731 and 7919 were males which resulted from the cross BALB/c♀×*M. spretus* ♂. Backcross (BC) mice were progeny of the cross (BALB/c×*M. spretus*) F₁♀×BALB/c ♂.

§ The *H-2* genotype was inferred from the monoclonal antibody reactivities. To our knowledge there is no official designation for *M. spretus* *H-2* haplotypes. For the purpose of this linkage study, no attempt has been made to distinguish between different *M. spretus*-derived *H-2* haplotypes; all are referred to by the letters *sp*. Note, however, that the 10-3.6-negative phenotypes observed for F₁ 8731 and backcross mouse 9349 probably reflect the presence of two or more distinct *I-A* alleles in the *M. spretus* *H-2* haplotypes followed in this study.

|| The *Ii* genotype was determined as shown in Fig. 1.

The β_2m -microglobulin genotype (β_2m) was determined by two-dimensional PAGE of rabbit anti-mouse- β_2m immunoprecipitates. The BALB/c (*a*) form is considerably more basic than the *M. spretus* form. No official allele designation has been made for *M. spretus* β_2m ; here we refer to the *M. spretus*-derived β_2m allele by the letters *sp*.

** The genotype at the albino (*c*) locus was inferred from the coat colour of the F₁ and backcross mice.

obtained from three F₁ females. To determine whether the gene encoding *I_i* might be linked to the *H-2* complex, backcross mice were scored for both their *Ii* and *H-2* genotype. We have designated the BALB/c allele for *Ii*, *I^a_i* and the *M. spretus* allele *I^b_i*. The *Ii* genotype was determined by two-dimensional PAGE of ³⁵S-methionine-labelled extracts (Fig. 1). To confirm that the spots identified as *I_i* in the extracts were indeed *I_i* chains, immunoprecipitates of Ia antigens from spleen cell extracts of *M. spretus*, F₁ and backcross mice were also analysed on two-dimensional gels. The variant spot in question was immunoprecipitated with Ia-specific monoclonal antibodies, thus demonstrating that it is in fact *I_i*. Representative immunoprecipitation results are shown in Fig. 2 and have been confirmed with several other *M. spretus* and F₁ mice as well as with all backcross progeny. The *H-2* genotypes of the backcross mice were determined by quantitative immunofluorescence (FACS) analysis using three monoclonal antibody reagents (Fig. 3). Confirmation of the *H-2* typing was obtained with an anti-*H-2* serum (B626, BALB/c anti-BALB.B, a gift from Dr David Sachs of the National Cancer Institute) as well as by two-dimensional PAGE analysis of *H-2* proteins immunoprecipitated with rabbit anti-mouse β_2m -microglobulin. The results of the *H-2* and *Ii* typing are summarized in Table

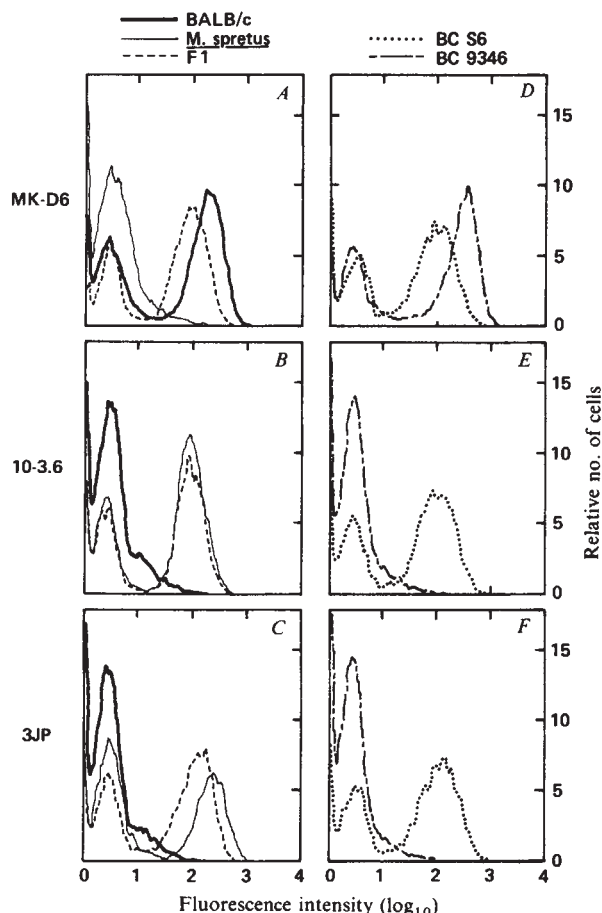


Fig. 3 Assignment of *H-2* genotype by analysis on the fluorescence-activated cell sorter (FACS). Representative fluorescence histograms generated by FACS are shown for BALB/c, *M. spretus*, F₁ and backcross mice. MK-D6 is an anti-*I-A^d* monoclonal antibody and does not react with *M. spretus* cells. 10-3.6 and 3JP (a gift from Dr Donal Murphy, Yale University School of Medicine) are both anti-*I-A* monoclonal antibodies that react with *M. spretus* but not with BALB/c cells. Red cell-depleted spleen cell suspensions (1×10^6 cells per sample) were stained by a 15-min incubation at 4°C with the appropriate monoclonal antibody followed by 15 min at 4°C with a fluorescein isothiocyanate-labelled γ -chain-specific rabbit anti-mouse IgG. Cells were analysed on a modified FACS II (Becton-Dickinson) equipped with a logarithmic amplifier.

1. Of the 12 backcross mice tested, 9 received non-parental combinations of *Ii* and *H-2* genes from the F₁ mother. These results indicate that, unlike the genes encoding Ia α and β chains, *Ii* is not closely linked to the *H-2* complex on chromosome 17.

During these analyses we were able to examine the possible linkage of *Ii* to sex (X chromosome), the albino (*c*) locus (chromosome 7)¹⁴ and the β_2m -microglobulin locus (chromosome 2)^{15,16}. The question of linkage to the β_2m -microglobulin (β_2m) gene is of particular interest because, like *I_i*, β_2m is a relatively non-polymorphic protein found in association with products of the *H-2* complex. Results summarized in Table 1 suggest that *Ii* is not closely linked to the β_2m -microglobulin gene or the albino locus, nor is it sex linked.

The *H-2* complex of the mouse contains numerous genes encoding immunologically important proteins, including *H-2* and Ia antigens which are involved in immune recognition. However, both classes of protein seem to require for their expression and/or function association with a non-*H-2*-linked polypeptide chain, β_2m -microglobulin for *H-2* antigens and *I_i* for Ia antigens.

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Stephen Beverley for introducing us to those stocks. We also thank Dr Michael Potter for generously supplying us with *M. spretus* and F₁ mice as well as some of the backcross mice used in this study; Lawrence D'Hoostelaere for assisting with these mice; Gene Filson for his operation of the FACS; and Sally Moran for her help in preparation of the manuscript. This work was supported by a grant from the Kroc Foundation and NIH grant AI 15732. The animals obtained through Dr Potter were bred at Litton Bionetics, Kensington, Maryland, in a fully-pedigreed colony maintained under NIH contract N01-CB-25584.

Note added in proof: Koch and coworkers have also recently obtained evidence that Ii is not linked to the H-2 complex. They found that production of mouse I_i in a mouse-hamster hybrid cell line does not require the presence of the mouse seventeenth chromosome¹⁹.

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A minor transplantation antigen detected by MHC-restricted cytotoxic T lymphocytes during graft-versus-host disease

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Transplantation of bone marrow can give rise to graft-versus-host disease when donor T lymphocytes, mismatched with the host for major histocompatibility (MHC) antigens, become sensitized and attack host tissues. However, graft-versus-host disease can also arise between donor and host with compatible MHC antigens but mismatched for a minor histocompatibility antigen^{1–3}. We report here on the occurrence of severe acute graft-versus-host disease in a male patient with acute myeloid leukaemia who had received bone marrow matched for MHC (HLA) antigens from his sister. Strong cytotoxicity of the post-transplantation (that is, donor) lymphocytes against the patient's pretransplantation lymphocytes was found. Thus, the transplanted lymphocytes differed in a non-HLA antigen from the patient. The possible role of this strong cytotoxic minor histocompatibility antigen in the development of graft-versus-host disease in man is being evaluated. Furthermore, with the use of cytotoxic T-cell lines, derived from the patient's 6 day effector cells, we are now able to type for it before grafting.

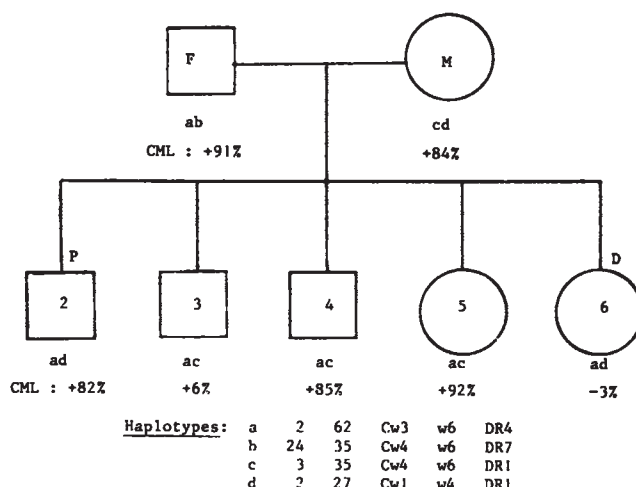


Fig. 1 Pattern of lysis in CML in the patient's family. The patient's cytotoxic effector cells (see legend to Table 1) were tested against his family members. F, father; M, mother; P (2), patient; D (6), donor; 3, 4 and 5 are siblings haploidentical to the patient. The % lysis (which represents the mean value of six experiments) at one effector: target cell ratio (50:1) is shown. a, b, c, d Delineate parental haplotypes.

Following transplantation, karyotype analysis confirmed that all the patient's post-transplantation lymphocytes were of donor origin. The initial experiment demonstrated that post-transplantation lymphocytes from the patient (HA) had strong cytotoxic activity, as measured by the cell-mediated lympholysis (CML) assay, against his own pre- but not post-transplantation lymphocytes⁴. The patient's cytotoxic effector cells (that is, the patient's post-transplantation peripheral blood lymphocytes sensitized *in vitro* for 6 days with pre-transplantation lymphocytes) used in this initial experiment also lysed two out of four randomly chosen control target cells (Table 1). Lymphocytes of the donor were not lysed.

These cytotoxic effector cells were then tested in the CML assay against target lymphocytes from the parents and three siblings (haploidentical to the patient); Fig. 1. Besides absence of cytotoxicity against the lymphocytes of the bone marrow donor, absence of lysis was repeatedly demonstrated against the lymphocytes of one out of three HLA-identical siblings which shared one HLA haplotype with the patient. As the cytotoxicity pattern in the patient's family showed a difference between HLA-identical siblings, we hypothesized that the target antigen is encoded outside the HLA region but the response to it is restricted by HLA.

In an attempt to identify the determinant, we examined the following polymorphic genetic systems in the patient's family which could be a marker for a minor histocompatibility antigen: (1) blood groups, including ABO, Rhesus, MN, P, S, K, Fy and Lewis; (2) complement polymorphic markers⁵; (3) immunoglobulin allotypic markers GM, AM and KM (ref. 6); (4) 13 intracellular enzymes: ACP1, ADA, AK1, ALAD, DIA2, ESD, GLO1, GPT1, PGD, PGM1, PGM3, PGP and SOD1 (ref. 7); (5) group Five system⁸; and (6) sex and chromosomal patterns. For none of these systems could we demonstrate a difference between either donor and patient before transplantation or between sibling 3 versus 4 and 5 which correlated with the CML results.

To investigate whether the recognition of the minor antigen 'HA' is HLA-restricted, as is the response to H-Y in HLA-A2-positive female aplastic anaemia patients⁹, a random panel analysis was performed. The cytotoxic effector cells, that is, patient's post-transplantation peripheral blood lymphocytes sensitized *in vitro* with pre-transplantation patient's lymphocytes were tested in the CML assay against more than 150 randomly chosen unrelated healthy individuals. The results (Table 2) showed an almost complete association with the HLA-A2 determinant but in addition, lysis of target cells which

Table 1 % Lysis obtained with post-transplantation effector cells of patient HA

Target cells	HLA phenotypes						% Lysis
	A	B	C	DR	SB		
Patient (pre-transplantation)	2	27	62	1	1.4	4.4	+59
Patient (post-transplantation)	2	27	62	1	1.4	4.4	-1
Bone marrow donor	2	27	62	1	1.4	4.4	-3
Unrelated individual	3 31	27	40	2.3	4		+5
Unrelated individual	1 32	8	44		3.7		-7
Unrelated individual	2 11	51	62	3	1.2		+26
Unrelated individual	2	7	27	2	2.6		+35

The effector cells (phenotype HLA-A2, A2, B27, Bw62, Cw1, Cw3, DR1, DR4, SB4) used throughout this study were patient's post-transplantation peripheral blood lymphocytes (that is donor cells) sensitized *in vitro* for 6 days with pre-transplantation patient's lymphocytes. These effector cells were tested against randomly-selected panel and family donors (see also Table 2, Figs 1, 2) as target cells. The CML assay used has been previously described in detail. Cytotoxicity in Tables 1-3 and Figs 1, 2 the amount of isotope released from the (^{51}Cr -labelled target cells) was determined and calculated according to methods described earlier¹⁶. All experiments were repeated at least twice at six effector to target ratios. Lysis at only one effector: target ratio (50:1, that is, $2.5 \times 10^5 : 5 \times 10^3$) is shown in this table. Positive and negative assignment was made on the basis of a 10% specific ^{51}Cr release value. Standard errors of the means of triplicates were always less than 5%. No lysis occurred when responder cells were tested against the relevant target cells after the following cultures: a, patient's post-transplantation lymphocytes as responder cells with the donor cells as stimulator cells; b, donor cells as responder cells with patient's post-transplantation lymphocytes as stimulator cells; and c, donor cells as responder cells with the patient's pre-transplantation lymphocytes as stimulator cells.

carried either the HLA-B27 or the HLA-Bw62 antigen was also found. All antigens belong to the HLA genotypes of donor and patient, that is, they are 'self' antigens. These results suggest that the response to the minor antigen is restricted to these 'self' HLA antigens. The panel study also showed that the minor antigen is found at a high frequency in the random population; 95.5% of the HLA-A2-positive, 20% of the HLA-B27-positive and 60% of the HLA-Bw62-positive panel donor cells tested showed significant lysis (Table 2).

The occurrence of an HLA-A2 variant in the patient's family seems unlikely to explain these results because cytotoxic T lymphocytes specific for an HLA-A2 variant¹⁰ did not lyse the patient's cells (pre- and post-transplantation) or those of his family (data not shown). Preliminary biochemical analysis showed no chemical differences between the patient's lymphocytes before and after transplantation (H. Ploegh, personal communication).

To further investigate the cytotoxic determinant, family studies were performed by assaying target cells derived from relatives of HLA-A2-positive panel members. The cytotoxic determinant segregated in 12 families with the haplotype carrying the HLA-A2 antigen. Furthermore, in two HLA-A/C cross-over families, the target determinant segregated with the HLA-A2 antigen. One example of such a family is shown in Fig. 2. Consequently, the minor transplantation antigen which

is seen in association with the HLA-A2 antigen shows both a high frequency in the panel and in the family analysis and a codominant inheritance. Only five HLA-A2-positive individuals, whose lymphocytes were not lysed, have been found so far, two from the family of the patient (Fig. 1) and three HLA-A2-positive panel members (Table 2). Family studies of non-HLA-A2-, but HLA-B27- or HLA-Bw62-positive panel members have still to be performed.

An attempt was made to identify whether or not the minor transplantation antigen which is recognized in association with HLA-A2 is distinct from those recognized by HLA-Bw62 and/or HLA-B27. Cold target cell inhibition studies (Table 3) and the T-cell clone analyses (data not shown) showed unequivocally that the HLA-A2-, B27- and Bw62-restricted T-cell subsets were all separate. Nevertheless, we have as yet no data to indicate whether or not the non-HLA antigen which is seen in association with HLA-A2 is the same as those seen in association with HLA-B27 and HLA-Bw62.

Our data suggest that we have defined an HLA-restricted minor histocompatibility antigen(s) that might be similar to that described earlier in mice^{2,3}. We have called this antigen HA. The restricting elements were the HLA-A and the HLA-B antigens of the patient's lymphocytes. The non-HLA determinant remains unidentified at present, but we assume that the parents are both heterozygous for this antigen with a high gene frequency, the bone marrow donor and sibling 3 (Fig. 1) being homozygous for the allele 'HA' which has a gene frequency of ± 0.07 if HLA-A2 is present.

Graft-versus-host reactions are mediated by subpopulations of donor T cells and can be attributed to non-MHC antigens. For example, peripheral blood lymphocytes of two female aplastic anaemia patients showed HLA-restricted H-Y killing in a CML assay. These observations argue for the influence of the male H-Y antigen as a non-MHC minor transplantation antigen^{9,11,12}. In agreement with this, sex-mismatched bone marrow grafts do less well than sex-matched grafts especially

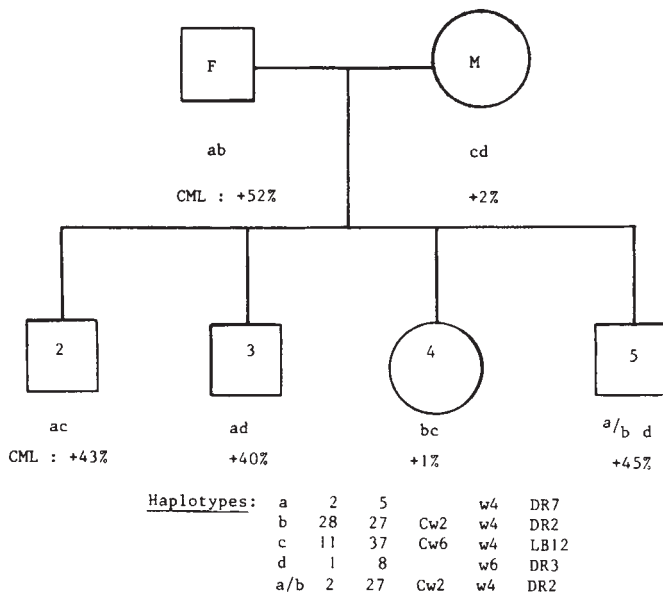


Fig. 2 Segregation pattern of the HLA-restricted minor histocompatibility antigen in an HLA-A/C cross-over family. The % lysis at only one effector: target cell ratio (50:1) is shown.

Table 2 Analysis of HLA-restricted anti-HA antigen lysis

	Target cells			
	Serological typing for			
	HLA-A2 ⁺ , B27 ⁺ , Bw62 ⁻	HLA-A2 ⁻ , B27 ⁺ , Bw62 ⁻	HLA-A2 ⁻ , B27 ⁻ , Bw62 ⁺	HLA-A2 ⁻ , B27 ⁻ , Bw62 ⁻
CML ⁺	72	2	11	0
CML ⁻	3	13	6	47

The level of lysis obtained against the HLA-B27- and HLA-Bw62-positive target cells was always lower than that obtained against HLA-A2-positive target cells. Target cells carrying more than one restricting element are not included in this table.

Table 3 Competitive inhibition experiments

⁵¹ Cr-labelled target cells	Cold inhibitors added	% Lysis
HLA-A2 ⁺ , Bw62 ⁻ , B27 ⁻	None	+99
	HLA-A2 ⁺ , Bw62 ⁻ , B27 ⁻	+39
	HLA-A2 ⁻ , Bw62 ⁺ , B27 ⁻	+99
HLA-A2 ⁺ , Bw62 ⁻ , B27 ⁻	None	+97
	HLA-A2 ⁺ , Bw62 ⁻ , B27 ⁻	+26
	HLA-A2 ⁻ , Bw62 ⁺ , B27 ⁺	+95
HLA-A2 ⁻ , Bw62 ⁺ , B27 ⁻	None	+58
	HLA-A2 ⁻ , Bw62 ⁺ , B27 ⁻	+19
	HLA-A2 ⁺ , Bw62 ⁻ , B27 ⁻	+55
	HLA-A2 ⁻ , Bw62 ⁻ , B27 ⁺	+54

Patient's cytotoxic effector cells (see legend to Table 1) were tested against target cells that were positive for only one of the restricting HLA antigens but which were all positive for the minor antigen 'HA'. The inhibitory capacity of non-labelled target cells carrying only one of the restricting elements plus the minor antigen was measured. The ratio labelled: unlabelled target cells was 10:1. The % lysis of effector:target ratio of 50:1 is shown. The competitive inhibition protocol has been described in detail¹⁶.

if the donor is a female¹³. The possible role of the MNSs blood group antigen system on the occurrence of graft-versus-host disease has been reported by Sparkes *et al.*¹⁴. Elkins *et al.*¹⁵ described the recognition of a human minor alloantigen after *in vitro* stimulation with allogeneic cells of lymphocytes derived from a multi-transfused patient.

We believe that our findings might be of importance in the understanding of the biological role of non-HLA transplantation systems and in its management in organ transplantation. The fact that the cytotoxic T lymphocytes described here were found in a patient suffering from severe acute graft-versus-host disease suggests that incompatibility for the HA antigen might have had a role in the induction of the disorder. At present, however, it is possible, using cytotoxic T-cell lines derived from patient's 6-day effector cells, to type for the strong cytotoxic minor histocompatibility antigen HA before grafting. Serotyping for HLA with alloimmune sera (together with mixed lymphocyte culture between donor and recipient) appears to be insufficient to determine all the cell interactions dependent on HLA, and CML typing with cytotoxic T lymphocytes induced after *in vivo* priming might provide important information.

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Only membrane-associated RSV *src* proteins have amino-terminally bound lipid

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The product of the Rous sarcoma virus (RSV) transforming gene, *src*, is a phosphoprotein of molecular weight (*M*_r) 60,000 (pp60^{src})¹ that interacts with cellular membranes via an 8,000 *M*_r amino-terminal hydrophobic domain^{2–6}, possibly after post-translational modification^{5,7,8}. Recently, it has been demonstrated that fatty acid is tightly associated with some membrane-bound proteins^{9–15}, including pp60^{src} (ref. 16). The fatty acid attachment site is located within the membrane-embedded region of the vesicular stomatitis and Sindbis virus glycoproteins^{11,13–15}. To test for a similar modification of the amino-terminal domain of pp60^{src}, we measured the incorporation of ³H-palmitic acid into pp60^{src} of cells that had been transformed by wild-type RSV or recovered avian sarcoma viruses (rASVs)^{6,17}, some of which have variant forms of pp60^{src}. We report here that membrane-associated pp60^{src} proteins encoded by either wild-type RSV or rASV 1441^{6,17} contain bound lipid. However, pp60^{src} proteins with amino-terminal size variations encoded by two different rASV isolates, rASV 157 and rASV 1702¹⁷, that behave as soluble, cytoplasmic proteins⁶, contain no detectable lipid. Furthermore, we observed that lipid association is temperature sensitive in cells infected with RSV mutant tsNY68¹⁸, whose pp60^{src} membrane association is temperature sensitive^{19–21}. These data support the role of lipid binding in the membrane association of pp60^{src} and suggest that the amino-terminal 8,000 *M*_r of pp60^{src} contains the lipid attachment site.

Although pp60^{src} appears to interact with cellular membranes via an amino-terminal hydrophobic domain, its predicted amino acid sequence does not contain any extensive stretch of hydrophobic residues within 8,000 *M*_r of the amino-terminus^{7,8}. Pulse-chase studies suggest that pp60^{src} is synthesized as a soluble protein that later becomes membrane-associated⁵, presumably by post-translational modification. The interaction of pp60^{src} with the membrane may be mediated by attachment of fatty acid¹⁶. To determine whether membrane-associated pp60^{src} contained bound fatty acid, transformed cells were radiolabelled in culture with ³H-palmitic acid and cellular extracts were immunoprecipitated with tumour-bearing rabbit serum as described in Fig. 1 legend. Cells were transformed by wild-type RSV or by recovered avian sarcoma viruses (rASVs), which are recombinants of transformation-defective mutants of RSV and the cellular *c-src* gene¹⁷. A single ³H-palmitate-labelled protein of 60,000 *M*_r that co-migrated with ³H-leucine-labelled pp60^{src} was detected in immunoprecipitates from cells transformed by the Schmidt-Ruppin strain, subgroup A, of RSV (SR-RSV-A) or rASV 1441, in which pp60^{src} is membrane-associated⁶. Since immunoprecipitates of extracts from cultures labelled in parallel with ³H-leucine contained other labelled viral proteins (Pr76, p27, and pp52^{2–4}, the proteolytic breakdown product of pp60^{src}), but only pp60^{src} was detected by ³H-palmitate labelling, it is likely that the ³H-palmitate labelling pattern is the result of fatty acid binding to pp60^{src} and not the conversion of the ³H label into amino acids. No ³H-palmitate labelling of RSV glycoproteins gp85 and gp37 was detected, although it has been reported that these proteins contain bound fatty acid¹³. However, the tumour-bearing rabbit serum used in these experiments does not immunoprecipitate detectable amounts of ³H-leucine-labelled gp85 or gp37 from RSV-transformed cells. The absence of ³H-palmitate label in

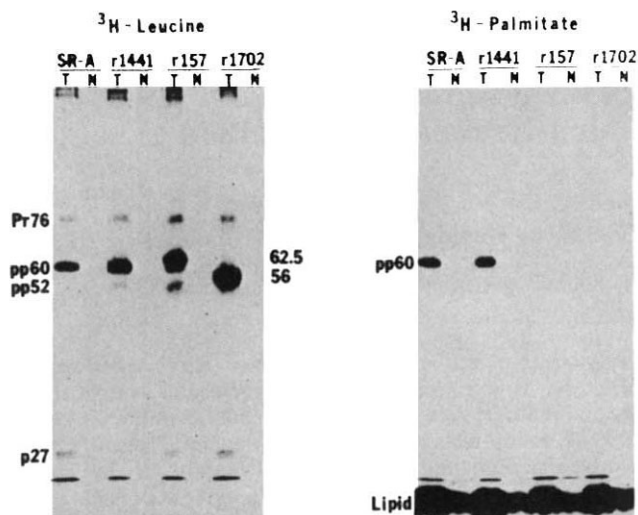


Fig. 1 Standard pp60^{src} proteins contain bound lipid, shown by ³H-palmitic acid labelling, but pp60^{src} proteins with amino-terminal alterations are not labelled with ³H-palmitic acid. Chick embryo fibroblasts were cultured and infected with Schmidt-Ruppin Rous sarcoma virus, subgroup A (SR-A), or recovered avian sarcoma virus isolate rASV 1441, rASV 157 or rASV 1702^{6,17}.

Methods: Transformed cells (100-mm dishes) were labelled for 16 h at 37 °C with ³H-palmitic acid 0.25 mCi ml⁻¹ or ³H-leucine 0.1 mCi ml⁻¹. Labelling with ³H-palmitic acid: [9,10-³H(N)]-palmitic acid (NEN, 15.2 Ci mmol⁻¹) in toluene was dried under nitrogen and then dissolved in 75 mM NH₄OH. Palmitic acid then was mixed with Dulbecco's modified Eagle's medium (DME) containing 5% calf serum and 5% tryptose phosphate broth. Labelling with ³H-leucine: cells were labelled with L-[4,5-³H(N)]-leucine (NEN, 59.2 Ci mmol⁻¹) in DME containing 10% of the normal concentration of leucine and 5% dialysed calf serum. Cultures were washed three times with cold phosphate-buffered saline and were then lysed in 1 ml cold 10 mM Tris-HCl (pH 7.2), 150 mM NaCl, 5 mM EDTA, 10% glycerol, 1% Triton X-100, 1% sodium deoxycholate, 100 kIU ml⁻¹ Trasylol, and 1 mM phenylmethylsulphonyl fluoride (buffer A). Lysates were scraped from the plate with a rubber policeman, incubated on ice for 10 min, and then clarified by centrifugation for 10 min at 15,000g. Aliquots of labelled cell lysates containing equal amounts of cell protein were immunoprecipitated with saturating amounts of tumour-bearing (T) or normal (N) rabbit serum for 1 h on ice. Immune complexes were adsorbed with protein A-Sepharose for 30 min on ice. The immunoprecipitates were pelleted, then washed three times with cold buffer A containing 300 mM NaCl and 0.1% SDS, and once with buffer A containing 10 mM NaCl and 0.1% SDS. Immunoprecipitates were resuspended in 125 mM Tris-HCl (pH 6.8), 2% SDS, 50% glycerol and 0.001% bromophenol blue, and boiled for 2 min. Samples were subjected to electrophoresis on a 10% SDS-polyacrylamide gel. Immediately after electrophoresis, the gel was dehydrated in dimethyl sulfoxide, impregnated with diphenyloxazole, rinsed with water and dried. To minimize any loss of ³H-palmitate label¹², buffers contained no -SH reducing agent, and SDS-polyacrylamide gels were not fixed after electrophoresis. Exposure of the fluorographed gel for 2 days yielded the ³H-leucine-labelled portion of the fluorograph, while exposure for 14 days yielded the ³H-palmitate-labelled portion of the fluorograph shown here. For quantitation of labelled proteins, protein bands of interest were excised from the gel, digested overnight in NCS tissue solubilizer (Amersham), and counted in scintillation fluid.

pp52^{src} (even on lengthy exposure of the fluorographed gel) suggested that the site of lipid attachment is within the amino-terminal 8,000 *M_r* of pp60^{src}. Sefton *et al.* have mapped the lipid attachment site to within the amino-terminal 18,000 *M_r* of pp60^{src} by partial proteolysis¹⁶. Based on quantitation of ³H radioactivity in leucine and palmitate-labelled pp60^{src} bands (Table 1), the specific activities of the radiolabels used, and the predicted amino acid sequences of SR-RSV-A and rASV 1441 *src* proteins^{7,8}, we estimate that SR-RSV-A and

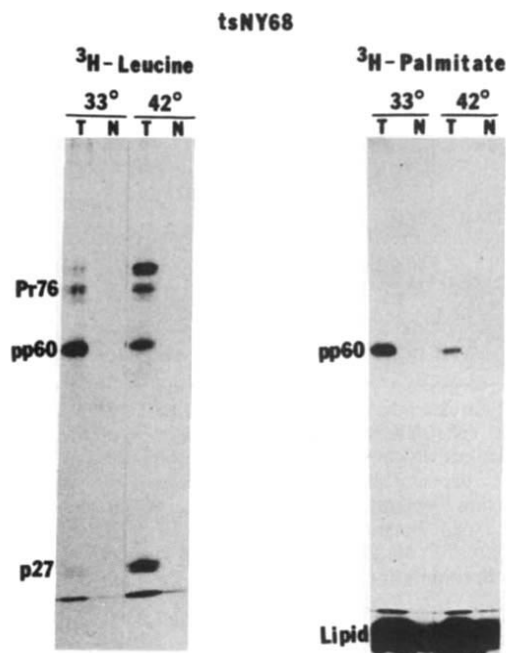


Fig. 2 ³H-palmitic acid labelling of tsNY68 pp60^{src} is reduced in infected cells maintained at the nonpermissive temperature. Chick embryo fibroblasts were infected with the temperature-sensitive RSV mutant tsNY68¹⁸ and maintained at the permissive (33 °C) or nonpermissive (42 °C) temperature. Cells were labelled for 16 h at the stated temperature with either ³H-leucine or ³H-palmitic acid. Labelled proteins were immunoprecipitated with tumour-bearing (T) or normal (N) rabbit serum and subjected to electrophoresis on a 10% SDS-polyacrylamide gel. The gel was processed for fluorography, and was exposed as described in Fig. 1 legend. pp60^{src} bands were excised for quantitation.

rASV 1441 *src* proteins contain no more than one molecule of lipid per molecule of pp60^{src}. It has been demonstrated previously that palmitate is the lipid moiety incorporated into fatty acid acylated proteins when cells are labelled with ³H-palmitic acid^{9-13,15,16}.

No ³H-palmitate label was detected in the 62,500 *M_r* *src* protein encoded by rASV 157 or in the 56,000 *M_r* *src* protein encoded by rASV 1702 (Fig. 1). In cells transformed by these rASVs, which have *src* protein size variations within 8,000 *M_r* of the amino-terminus¹⁷, the *src* proteins behave as soluble, cytoplasmic proteins⁶. These data also suggest that the lipid attachment site lies within 8,000 *M_r* of the amino-terminus of pp60^{src} and that lipid binding may indeed function to anchor the protein in the membrane. Since rASV 157 and rASV 1702 also show greatly attenuated *in vivo* tumorigenicity^{6,17}, lipid binding to pp60^{src} may have a role in promoting tumour formation.

To further test the correlation between lipid binding and pp60^{src} membrane association, ³H-palmitate labelling of pp60^{src} was examined in cells infected with the RSV mutant tsNY68¹⁸ maintained at the permissive and nonpermissive temperature and the results of that experiment are presented in Fig. 2. The bulk of tsNY68 pp60^{src} is not membrane-associated at the nonpermissive temperature¹⁹⁻²¹. Quantitation of labelled pp60^{src} bands from the gel shown in Fig. 2 indicated that the ratio of ³H-palmitate to ³H-leucine incorporated into pp60^{src} was reduced approximately threefold at the nonpermissive temperature relative to that at the permissive temperature (Table 1). This result is consistent with the three- to fourfold reduction in the amount of membrane-associated pp60^{src} observed at the nonpermissive temperature^{19,21}. The mutant pp60^{src} may bind less lipid because of a conformational change affecting the amino-terminal region of the protein.

The experiments described here cannot determine whether lipid binding is required before pp60^{src} membrane association

Table 1 Quantitation of ^3H -leucine and ^3H -palmitate labelled pp60^{src}

Infecting virus	Temperature	^3H -leucine pp60 (counts per 20 min)	^3H -palmitate pp60 (counts per 20 min)	^3H -palmitate c.p.m./ ^3H -leucine c.p.m. ($\times 10^{-2}$)
SR-RSV-A	37 °C	157,536	5,300	3.364
rASV 1441	37 °C	219,972	5,984	2.720
rASV 157	37 °C	386,316	190	0.049
rASV 1702	37 °C	495,696	246	0.050
tsNY68	33 °C	163,776	7,965	4.863
tsNY68	42 °C	85,524	1,552	1.815

pp60^{src} bands (or the region of the gel corresponding to *src* protein) were excised from the gels shown in Figs 1 and 2, digested overnight in NCS tissue solubilizer, and counted in scintillation fluid.

or if lipid binding occurs after membrane binding of pp60^{src}. Studies on the vesicular stomatitis virus (VSV) glycoprotein, which is acylated on a transmembrane hydrophobic domain near its carboxy-terminus, indicate that the fatty acid modification occurs before transport of the glycoprotein to the cell surface and may be required for stable interaction with the plasma membrane^{9,11,14,22,23}. But since pp60^{src} is translated on free polysomes^{24,25}, there is no *a priori* reason to assume that its biogenesis in any way resembles that of viral transmembrane glycoproteins. Recently, it has been demonstrated that the plasma membrane-associated transforming proteins of Harvey murine sarcoma virus and Abelson murine leukaemia virus also contain tightly bound fatty acid¹⁶.

The precise chemical nature of the lipid association with pp60^{src} has not been determined, since the incorporation of ^3H -palmitate into pp60^{src} is extremely low. The lipid label in pp60^{src} has been reported to be insensitive to hydrolysis by NH_2OH or mild methanolic KOH ¹⁶, suggesting that the lipid is not esterified (to serine^{9,14,23}) as in VSV or Sindbis virus glycoproteins^{9,11,12-15}. The linkage is also unlikely to be a thioether bond to a cysteine residue, as in the *Escherichia coli* outer membrane murein lipoprotein²⁶, since the predicted amino acid sequence of SR-RSV-A pp60^{src} contains no cysteine residue within 8,000 M_r of the amino-terminus^{7,8}. The lipid may be bound to pp60^{src} through an amide linkage as in the *E. coli* lipoprotein²⁶ or bovine cardiac muscle cyclic AMP-dependent protein kinase²⁷. Regardless of the details of the lipid linkage, lipid binding and pp60^{src} plasma membrane association appear to be highly correlated. The mutants used in this study allow the lipid attachment site to be mapped to the amino-terminal 8,000 M_r of pp60^{src}. The role of the bound fatty acid in pp60^{src} function remains to be elucidated. It has been suggested that bound lipid can enhance the interaction of a protein with the plasma membrane by anchoring it within the lipid bilayer^{9-16,22,23,27}. Our studies on the consequences of altered membrane interaction of pp60^{src} on *in vivo* tumorigenicity⁶ and the results presented here suggest that lipid binding to pp60^{src} may provide a membrane anchorage function in promoting tumorigenicity.

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Sequence homology between Lac and Gal repressors and three sugar-binding periplasmic proteins

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Many proteins consist of several independent folding units or domains, each specifying a different function¹. Repressor proteins such as Lac or λ cI carry small N-terminal domains which recognize DNA sequences and larger C-terminal domains which are required for effector recognition and/or oligomerization²⁻⁴. The native periplasmic metabolite-binding proteins consist of short membrane-recognizing signal sequences⁵ and larger C-terminal metabolite-binding domains which also recognize membrane-bound proteins involved in transport⁶ and chemotaxis⁷. The DNA-recognizing domains of many repressors are homologous⁸⁻¹², as are the sugar-recognizing periplasmic proteins¹³. Here I demonstrate that the sugar-binding domains of the Lac and Gal repressors are homologous with the sugar-binding domains of three periplasmic proteins.

Recently, a striking sequence similarity between the N-terminal domains of some repressors has been demonstrated⁸. This sequence homology probably indicates a similar mode of DNA binding and recognition by α -helical arms in the major groove of DNA⁸. The list of homologies⁹⁻¹² includes the Lac and Gal repressors, Lys repressor, LexA repressor, λ , P22 and 434 cI repressor, λ , P22 and 434 cro protein and λ cII. Whereas all the repressors mentioned above have homologous N-terminal domains, homologies in the C-terminal domains have only been demonstrated in two groups: the Lac and Gal repressors¹¹ and the cI and LexA repressors^{9,12}. The cro proteins comprise just one, DNA-binding, domain.

In their native state the periplasmic proteins consist of an N-terminal membrane-recognizing domain, the signal sequence⁵ and a C-terminal part which may comprise several domains. The N-terminal signal sequence guides the protein

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AraBP 147 T A R R R T T G S M D A L K A A G F P E K Q I Y Q V P T K S N D I P G A F 183
GalBP 155 - A K E R T T T Y V I K E L N D K G I K T E Q L - Q L D T A M W D T A Q A K 185
RibBP
GalR 190 D A E D R L Q G Y Y D A L A E S G T A A N D R L V T F - - - G E P D E S G 223
LacR 193 S A R L R L A G W H K Y L T R N Q I Q P I A E R E - - - G D W S A M S 224

AraBP 184 D A A N S M L V Q H P E V K H W L I V G M N D S T V L G G F V R A T E G Q G 220
GalBP 190 D K M D A W L S G P N A N K I E V V I A N N D A M A M G A V E A L K A H N 226
RibBP
GalR 224 G E Q A M T E L L G R G R N F T A V A C Y N D S M A A G A M G V L N D N G 260
LacR 225 G F Q Q T M Q M L N D G I V P T A M L V A N D Q M A L G A M R A I T E S G 261

AraBP 221 F K A A D I I G I G I N G V D A V S E L S K A Q A T G F Y A G S L P S P 257
GalBP 227 - - - - K S S I P V F G V D A L P E A L A L V K S G A L A G T V N D A 258
RibBP
GalR 261 I D V P G - - E I S L I G E D D V L V S R Y V R P R C T T V R Y P I V T M 295
LacR 262 L R V G A - - D I S V V G Y D D T E D S C Y I P P L T T I K Q D F R L L 296

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Fig. 1 Alignment of protein sequences of the arabinose-binding protein (AraBP), the galactose-binding protein (GalBP), the ribose-binding protein (RibBP), the galactose repressor (GalR) and the lactose repressor (LacR). ---, Arbitrarily introduced deletion; . . ., sequence not determined. The periplasmic proteins are aligned according to ref. 13, the repressors according to ref. 11.

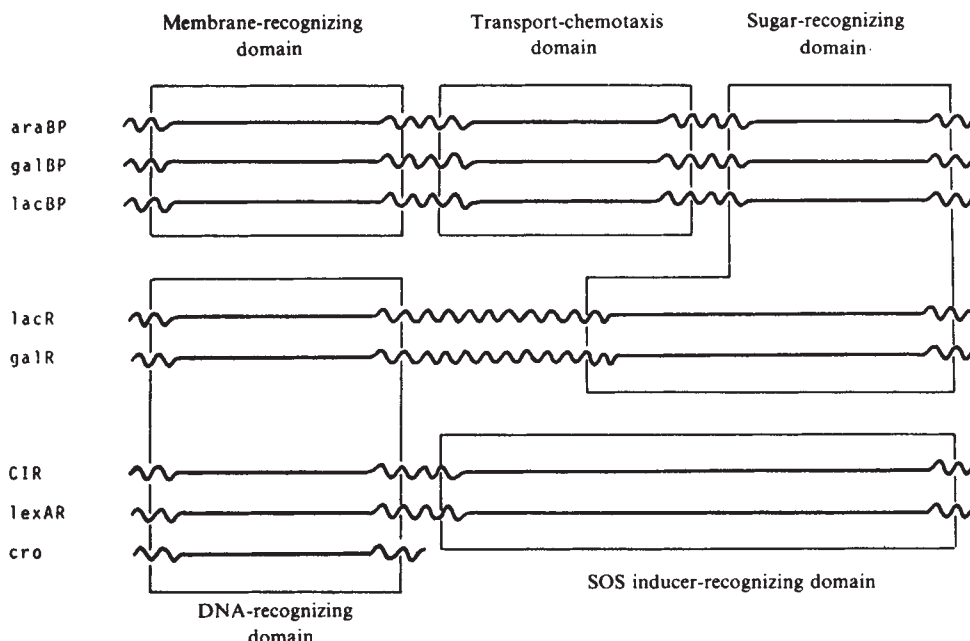


Fig. 2 Schematic representation of building blocks shared by repressors and transport proteins. Similar building blocks or domains are shown in separate boxes. Five types of building blocks are shown: the membrane-recognizing domain or the signal sequence, the DNA-recognizing domain, the domain(s) involved in recognition of membrane proteins needed for transport and chemotaxis, the sugar-recognizing domain(s) and the SOS inducer-recognizing domain(s). The sugar-recognizing domain(s) of repressors also contain sites allowing self-aggregation¹⁶. The SOS inducer-recognizing domain recognizes the signals leading to LexA induction and self-aggregation. All proteins but cro consist of at least two domains.

through the inner membrane of *Escherichia coli* into the periplasm, then it is clipped off proteolytically. The periplasmic proteins which bind galactose, ribose and arabinose have recently been sequenced and found to have homologous structures¹³. This led me to compare the sugar-binding domains of the Lac and Gal repressors with those of the galactose-, arabinose- and ribose-binding periplasmic proteins. I used the known homologies between Gal and Lac repressor cores¹¹ to look for homologies in the periplasmic proteins. Figure 1 shows that homologies exist between all five proteins. The homologies suggest that the Lac and Gal repressors and the sugar-binding proteins have similar three-dimensional structures in the homologous region.

Figure 2 gives a schematic view of the homologies found in various domains of the repressors and transport proteins mentioned above. It illustrates the use of the molecular building blocks found in living systems¹⁴. But how did the building blocks arise? Do the homologies indicate convergent or divergent evolution? The latter question cannot be answered at present. Divergent evolution would require an effective mechanism of joining genes coding for different functional protein units such as that found in eukaryotic cells¹⁵.

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In praise of lesser books

Classic textbooks bring renown to their authors, but students rarely read them. Walter Gratzer argues that publishers would do well to woo a new breed of textbook writer.

DOROTHY Parker is supposed to have said in an address to the New York Horticultural Society: "You can lead a horticulture but you can't make her think". So it is with students. The universities, at least in Britain, are engines for the education of the self-educating: the politician whose entry under education in *Who's Who* reads "self-educated at Eton and King's" many not have been joking. Those without the gift become the silent majority of the lecture room, those rows of disembodied uvulas, victims of a conspiracy of disregard; for our academics adhere to the illusion that they are members of a community of scholars, entrusted with the propagation of their field of scholarship by way of research, and incidentally with the reproduction of their kind.

The first-year undergraduate, bereft of the intensive teaching he will have had in the sixth-form, is apt to feel the more aggrieved when he discovers that the sources recommended by his lecturers are not substitutes for the excellent range of tried and dependable textbooks that will have been his companions through the preceding years. More, he will be expected to learn primarily from the most anachronistic and discredited of all the instruments of instruction, the lecture. Dr Johnson hit the nail on the head as always. "People" he wrote "have now a days got a strange opinion that every thing should be taught by lectures. Now, I cannot see that lectures can do so much as good as reading the books from which the lectures are taken".

So what of these books? Most academic scientists cleave to certain classic texts, on which very often they were brought up. Everyone can identify a number of magisterial works, many of which, even in an active subject, may endure for 50 years and more. Nearly always, they are written by luminaries in their fields, and at best they may throw a new perspective on an entire discipline and invest it with new life and excitement. The intellectual impact of such legendary works is often enormous and their influence may pervade the working lives of generations of scientists. Not long ago a leading theoretical chemist said of one celebrated textbook that its influence had set chemistry back 20 years. It is no mean book that can attract such obloquy, even allowing for a dash of *odium theologicum*. The effects of some of these books on the professional personae of scientists can perhaps best be compared to those of Spock's baby books on the per-

sonalities of Americans — first, second and third edition babies, brought up in accordance with the different precepts on toilet training enunciated in successive revisions.

A classic, according to Mark Twain, is something that everyone wants to have read but nobody wants to read. Most undergraduates, I suspect, derive little profit or pleasure from the classic textbooks, for these are not written with the typical student in mind. They are conceived, I imagine, with an eye to posterity and as a bid for a posthumous academic progeny and with it immortality for the culture-genes, in an age in which citations of publications in the primary literature fall off according to a first-order decay law, with a half-time of a year or so. Successful scientists are seldom plagued by excessive modesty, and anyone who doubts that the prospect of oblivion for their work holds the liveliest terrors might reassure himself by recalling Bertrand Russell's story about the recurring nightmare that visited him in middle-age: he saw before him the Recording Angel moving along the library shelves, selecting those few books that would be spared from the fire on the Final Day. Each time he would observe with agitation that the angel had reached the letter R, and that his hand was hovering above *Principia Mathematica*; and then he would wake, trembling.

If I do not misjudge them, university teachers might well suggest that it is no fault of theirs if undergraduates are not available who are worthy of their textbooks. Bertolt Brecht's rejoinder to the complaint from the East German regime that the performance of the country's workers was unworthy of the Government's economic plan was to ask why the Government should not then dissolve the people and elect another. Academics are bred and selected for their prowess at research and nothing else, and, as I have suggested, neither they nor the system have much patience with the concerns of students, except the few that the system will claim for its own. If you do not believe me, here is a higher authority on the subject, Cardinal Newman, writing a century ago:

To discover and to teach are distinct functions; they are also distinct gifts, and are not commonly found united in the same person. He, too, who spends his day dispensing his existing knowledge to all comers, is unlikely to have either leisure or energy to acquire new. Common sense of mankind has associated the search after truth with seclusion and quiet. The greatest

thinkers have been men of absent minds and idiosyncratic habits, and have more or less shunned the lecture room and public school.

I would further suggest that the chief aim of the university lecture is more to establish the ascendancy of the lecturer over the Great Unwashed before him than to dissipate his hard-won knowledge. Why otherwise has the lecture survived as an institution so many centuries after the Venerable Bede amazed his contemporaries with his ability to absorb the contents of a book without articulating it aloud? It was, I believe, another mediaeval divine who said: "The vanity of teaching often tempteth a man to forget that he is a blockhead".

One of the two authors of a highly successful series of American chemistry texts accounted for their popularity with students by his resolve, and that of his colleague, to concentrate their efforts on explaining the subject to even the dullest student, rather than to show off their own knowledge — something to which the very character and training of most academics predisposes them. Few people take kindly to being persuaded that they are not after all very bright, nor will they easily forgive the bringer of such tidings. Professional teachers are less likely to offend in this way than academic research workers, and students will reward them by buying their books.

There are now a number of admirable university textbooks, written by teachers, professional textbook writers or others who have never held a test-tube, even, in at least one case, a journalist. It may be that we are witnessing the emergence of a new craft. The products are not monuments of scholarship that illuminate the field anew; their object is more modest but no less estimable, and they probably find little favour among university lecturers, but if they work for the student in the modern education mill, he will vote with his wallet. There are of course striking exceptions to my rule, even books of quality written, against all the odds, by committees, as indeed the pages that follow will show; in any case the minority of students with an academic bent, as well as research students and the rest of us, have our special needs. I suspect, however, that most new books satisfy neither one group nor the other, and vanish instantly into that bourn from which no book returns as a second edition. If I were a publisher in quest of your five-edition man, I rather think it is the new professionals that I should look to rather than the scientific magi; and I should keep in mind how one of the most successful of all writers summed up her approach to her craft, the romantic novelist, Ruby M. Ayres, quoted in her obituary in *The Times*: "First I fix the price. Then I fix the title. Then I write the book". □

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Rating in biological science

E.C. Cox and R.M. May

Biology, 4th Edn. By Helena Curtis.

Worth: 1983. Pp.1,071. \$27.95.

Biology, 2nd Edn. By Karen Arms and Pamela S. Camp.

Saunders: 1982. Pp.935. \$27.95, £19.50.

The Study of Biology, 4th Edn. By J.J.W. Baker and G.E. Allen.

Addison-Wesley: 1982. Pp.971. \$26.95, £14.95.

The Science of Biology, 5th Edn. By P.B. Weisz and R.N. Keogh.

McGraw-Hill: 1982. Pp.1,009. \$27.50, £21.25.

Biology: The Essential Principles. By Tom M. Graham.

Saunders: 1982. Pp.575. \$27.95, £18.95.

Elements of Biology, 3rd Edn. By C.K. Levy.

Addison-Wesley: 1982. Pp.550. \$23.95.

IN 1980, we gave a comparative review of seven introductory biology texts, including the previous editions of Curtis and of Arms and Camp (*Nature* 284, 106; 1980). Like these earlier texts, and indeed like essentially all introductory biology texts, the present six books are organized along hierarchical "little-to-big" lines; they begin with chemistry and molecular biology, proceed to cellular, organismal and population biology, and end with chapters on human ecology.

Our review of the fourth edition of Curtis is based on the first 19 chapters (molecules through cells) and the last 11 chapters (evolution and ecology). This book goes from strength to strength, and we think it is clearly the best text for a student who is just beginning biology, or who is not too well prepared in science. The graphics continue to be superb, both in design and execution; no other text book comes close to achieving the same quality. This shows, especially, in the standard of the electron micrographs (which are difficult to reproduce under the best of circumstances); the micrographs are also correlated well with interpretive drawings, much as in Keeton's *Biological Science* (for review see *Nature* 289, 714; 1981) and earlier editions of Curtis. The writing style and organization are also consistently excellent — the prose is easy to understand and flows well.

This fourth edition embodies a substantial amount of reorganization and revision, particularly in the sections on evolution, population biology and ecology, which are now, in our opinion, the strongest such sections in any introductory text. The overall result is a book that is remarkably up to date, with many references to papers or advanced texts published in 1982 and 1983. This comment may be unfair to the other authors, since we are reviewing a pre-publication version of Curtis (and not even all of that), but we think Curtis's virtues go beyond this small temporal advantage. The text places less emphasis on experiments than we do in introductory teaching. It is, however, likely that the best way to keep things at the right level, while being com-

prehensive, is to stick to the "take home lessons".

The material in Arms and Camp has also been significantly reorganized. The original sixth and final section on evolution and ecology has undergone mitosis, and the new flow pattern — cell, information coding and transfer, evolution, diversity, animal biology, plant biology, ecology — is an improvement. Later printings of the first edition had already abandoned the double-column format for a single-column one, and in combination with other design changes and a simpler table of contents this gives the second edition a less forbidding air without diminishing its intellectual excellence. This text is somewhat more comprehensive than Curtis (especially on plant biology, one of its strengths) and in places goes deeper. For the serious and well-prepared student, Arms and Camp could be ranked above Curtis, though we think it remains below Keeton; although a physically beautiful book, it does not quite have the shine of Curtis or Keeton.

Also at the "high" end of the range — that is, in competition with Keeton — is the text by Baker and Allen. It is somewhat more comprehensive than Arms and Camp, but significantly less beautifully produced, and on balance we would rank it (in its class) with Arms and Camp, behind Keeton and a bit ahead of Curtis. The authors emphasize their plan to discuss experiments in detail, and to draw distinctions wherever possible between experimental facts, theories, conjecture and so on. In this aim they are successful, although on occasion their conscientiousness in distinguishing between alternative hypotheses when the data admit more than one interpretation can become laboured. We liked the discussion of basic chemical facts and the structure of water, and we enjoyed the supplements added to the introductory chapters. The treatment of thermodynamics and equilibrium, however, was perhaps a bit cursory for a comprehensive text of this kind. The sections on evolution and evolutionary patterns are excellent, and those on ecology are good, though some contentious ideas

(for instance, about the "Adaptationist Program") are presented uncritically. Several "boxed" essays are based on Gould's stimulating essays, and students will like them. The book comes with an extensive bibliography, although few of the references date beyond 1978.

Weisz and Keogh also appear to be aiming at serious students. This book focuses on macroscopic phenomena more than the other books, and emphasis is placed on the environment and the various problems that pollution has caused. The initial chemistry is solid, but the details of metabolism, molecular genetics and biochemistry are a bit sketchy. Various broadly ecological case-studies are offered, but the coverage of basic population biology and ecology is perfunctory. The sources cited for further reading rarely go beyond 1977.

The books by Graham and by Levy are pitched to relatively unprepared students. Graham's text is slightly the more comprehensive. It presents a somewhat dated "received wisdom" in an unexciting way, although some students may enjoy the emphasis on human functions. The ecology and evolution sections, in particular, read like a 20-year-old high-school text. Rarely are experiments discussed, and a large number of the illustrations are taken (admittedly with acknowledgement) from other introductory texts. We cannot complain that the readings are dated, because there are none.

Levy's text is, in parts, a substantial revision of the second edition, although the molecular biology remains quite out of date. This book looks dull beside some of the competition; the prose is dry and the graphics are often crude. The treatment of ecology and evolution is scantier than Graham's, except for the closing chapter on the human impact. The reading lists are not particularly good.

In all, we see several strong contenders at the high end, while Curtis seems streets ahead at the low end (and is unusual in also being competitive right across the spectrum). As a group, the books are better written and more error-free than those we reviewed in 1980 — less trendy language, less self-indulgent preaching, less advice on how to run your sex life. Perhaps the tenor of the times is changing, but more probably we are seeing the statistical effects of small sample sizes.

The debate about "Scientific Creationism" has left no scars on these pages. All of the authors give adequate space to evolution, and some use it as an organizing

Textbook supplement — prices

Where appropriate, both dollar prices pertaining in the United States and sterling prices for the United Kingdom are given in the bibliographical details for each book. Export prices will generally be higher. If a dollar or sterling price is not cited, the book is not available in one of the two countries. However readers should check both price and availability of books before ordering.

theme for their books. Curtis, in particular, devotes her Chapter 46 to an analytical survey of "The Evidence for Evolution". Only Curtis and Graham list "Creation" in their index, and none of the six books gives any account of contemporary quarrels with creationists. This may be the right approach. But we commend to all who teach introductory biology the excellent account of such quarrels, past and present, to be found in Luria, Gould and Singer's *A View of Life* (for review see *Nature* 295, 479; 1982).

We ended our 1980 review by noting that the prices of the seven texts were all approximately the same (ranging from \$16.50 to \$20). The present texts remain roughly equal in price (\$24 to \$28, representing an average inflation rate of 12 per cent per annum). Although the economic forces underlying this effective parity in price are understandable, the phenomenon is

remarkable when one considers the substantial differences in quality of production and quality of professional effort among these books. Why do the dozen or more less-excellent books survive, some of them going through edition after edition? A partial explanation is suggested by a very rough calculation that several millions of dollars in profits accrue annually from the sale of introductory biology texts, so that capture of less than one per cent of the market can be financially rewarding. Whatever the market forces, they serve us all well when they continue to produce, relatively cheaply, books of the quality of Keeton, Curtis and the others at the top of the range. □

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Before the bridges are built

Robert H. Smith

Insect Herbivory.

By I.D. Hodkinson and M.K. Hughes.
Pp.96.

Modelling. By John N.R. Jeffers. Pp.80.
Animal Population Dynamics.

By R. Moss, A. Watson and J. Ollason.
Pp.80.

Chapman & Hall: 1982.

Each book £2.95, \$6.50.

STUDENTS of ecology in the 1950s and 1960s were reared on a diet based mainly around Odum's *Fundamentals of Ecology* (Saunders, 1953); in the following decade students would more likely have had to digest either Krebs' *Ecology* (Harper & Row, 1972) or Ricklefs' *Ecology* (Nelson, 1973), but already there were appearing specialist texts to supplement the basic fare. The Institute of Biology series *Studies in Biology*, published by Edward Arnold, set off to a good start in 1966 with Phillipson's *Ecological Energetics* and now includes several ecology titles. Publishers Chapman & Hall have entered the 1980s with a new series, *Outline Studies in Ecology*, and it now seems to be accepted that ecology students are recommended a number of smaller books on specific topics rather than a single, comprehensive text. How good a job do these short texts do?

Insect Herbivory considers what plants can provide insects with, how insects are adapted to herbivory, and what the ecological consequences are. The book is well produced with an extensive bibliography (222 references for less than 60 pages of text) and to me, a non-specialist, it seemed a very useful introduction to insect-plant interactions.

Modelling is based around six questions,

the two most pertinent being "Why do I need a model?" and "How do I know when to stop?". The book is a clearly written summary of the technology of ecological modelling as seen by John Jeffers and is necessarily a personal overview, but it contains much wisdom that would benefit any ecologist, whether student or teacher. Sadly many of the models given as examples are described too briefly to be of much use to students, and not all of them are referenced. An appendix contains the checklist of questions for intending modellers published by the Institute of Terrestrial Ecology.

I found *Animal Population Dynamics* a most enjoyable read, but it is unfortunately severely flawed as a student text. The style is free-flowing and almost conversational, which is fine except when the excessive use of "this" and "these" leads to ambiguity. Considerable stress is laid upon behavioural mechanisms of population regulation and on the possibility that rapid genetic change may often be bound up with population fluctuations, but the majority of second-year undergraduates would be unable to evaluate the validity or generality of the arguments. One figure (4.7) has an unlabelled axis and another (7.1) uses undefined shading conventions — all right for me as I had read the original paper, but confusing for students. It is a pity that this potentially exciting textbook was spoilt by lack of attention to detail.

The authors of *Animal Population Dynamics* finish their book with the hope that "what we have written today, you will disprove tomorrow". Perhaps the role of these specialist texts is to act as stepping stones until they can be kicked away and replaced by a bridge linking different areas of ecology in an acceptable synthesis; the stepping stones will suffice for the time being. □

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Populations of all sorts

Michael B. Usher

Mathematical Methods of Population Biology.

By F.C. Hoppensteadt.

Cambridge University Press: 1983.

Pp.150. Hbk £15, \$29.95;

pbk £6.50, \$12.95.

Wildlife Population Ecology.

Edited by James S. Wakeley.

Pennsylvania State University Press:

1982. Pp.450. Hbk £14.85, \$24.10;

pbk £9.60, \$15.55.

A FEW biologists view population biology more as a branch of applied mathematics, whilst others see the subject as a respectable form of natural history. These extreme attitudes are evident in the two books under review.

Mathematical Methods of Population Biology is a very concise book which covers only a few topics. Mathematically-unsophisticated biologists will have some difficulty with the first and second chapters, and will find the final chapter especially tough going. The book starts with population dynamics, looking at models in refreshingly new ways. It progresses through some Matrix models to Markov chains applied to bacterial and human genetics, and then to a short chapter on perturbation methods which paves the way for a discussion of a number of dispersal and diffusion processes.

Little concession is made to the general lack of mathematical ability amongst biologists: a trivial example is the statement (p.35),

$$\lambda_1^2 + 1 = \lambda_1 + 1 + 1 = \lambda_1 + 2,$$

when, on the previous page,

$$\lambda_1 = (1 + \sqrt{5})/2.$$

Care must be also exercised in taking statements at their face value as there are mistakes, for example in the transposition of *a* and *b* in the formulae on page 29.

Frustration with having to dip into a variety of different journals led James Wakeley to bring together a collection of articles, reproduced in facsimile as *Wildlife Population Ecology*. Twelve papers deal with birds, and the remaining 19 either with mammals or mammal-based topics. The book is divided into two parts. The first considers the intrinsic components of populations — birth and death processes, dispersal, population growth and cycles. The second brings together some of the extrinsic factors that influence populations — the effects of climate, predators and competition. The distinction between the two parts is, however, somewhat fuzzy since physiological stress and behaviour fit comfortably into neither part.

Both of these textbooks have serious defects. *Mathematical Methods of Population Biology* is too condensed,

does not define mathematical formulations or expressions clearly enough and, biologically, is very patchy in its explanations. For example plasmids are not described at all, whilst the accounts of Mendelian genetics and schistosomiasis are far too simple. There are disappointingly few references, especially to real biological examples, although a series of exercises, with solutions, is included.

The problem with *Wildlife Population*

Ecology is that it is essentially unedited. The usefulness of the collection would have been increased no end if a substantial, critical analysis of the papers had been included; as it is, the editor contributes only two pages of commentary. Also, this book suffers from having no index, an omission for which I see no excuse. □

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A farewell to Chinese metaphysics

J.S. Jones

Population and Evolutionary Genetics: A Primer.

By Francisco J. Ayala.

Benjamin/Cummings: 1982. Pp.263.

\$13.95, £11.90.

Evolutionary Principles.

By Peter Calow.

Blackie/Methuen: 1983. Pp.116.

Hbk £13.95, \$35; pbk £6.95, \$15.95.

EVOLUTIONARY biology ought to be — but too often is not — the child of a marriage between ecology and genetics; a description of genetic changes in populations in terms of the ecological properties of each genotype. Strangely enough, the enormous advances made by its parental sciences have scarcely been reflected in much of the modern theory of evolution. Instead this remains obsessed with its own history, and the controversies which fill evolutionary texts today — random or directed change; gradual or sudden evolution; and the species, the group, the individual or the gene as the unit of selection — are those which occupied Haldane, Fisher and even Darwin himself. There is a synthesis between evolutionary genetics and evolutionary ecology only in the sense that Dickens' encyclopaedist synthesized his article on Chinese metaphysics from those on China and on metaphysics.

Each of these texts gives a very different view of modern evolutionary theory. That of Ayala is not new, as two-thirds of it is taken directly from the very successful *Modern Genetics* by Ayala and Kiger (Benjamin/Cummings, 1980). It gives a clear and straightforward account of quantitative theories of mutation, natural selection, genetic drift, inbreeding and multifactorial inheritance, together with a balanced treatment of modern views of speciation. The book takes most of its examples from work on *Drosophila*, and, as is reasonable in an introductory text, avoids many of the most controversial areas of evolutionary biology. It is more concerned with the genetics than with the ecology of evolutionary change.

Evolutionary Principles has a much less traditional approach. In a rather bewildering

succession Calow discusses the various controversies of evolutionary theory: the adaptationist programme; selfish DNA; the evolution of sex and of life history strategies; group and kin selection; cladistics; punctuated equilibria, and the developmental genetics of zebra stripes. His treatment is outstandingly up to date, as a third of the references cited have been published since 1980. To fit all this into a hundred pages of text leads to a certain

Depth in ichthyology

Alwyne Wheeler

Biology of Fishes.

By Q. Bone and N.B. Marshall.

Blackie/Methuen: 1982. Pp.262.

Hbk \$39.95; pbk £11.95, \$25.

Fishes: An Introduction to Ichthyology.

By Peter B. Moyle and J. J. Cech Jr.

Prentice-Hall: 1982. Pp.580.

\$33.95, £27.15.

FISHES are the most numerous group of vertebrates, outnumbering mammals, birds, reptiles and amphibians by at least two to one. With some 20,000 species the variations in fishes' body form and life style are enormous, and they have succeeded in colonizing virtually all the living space available to them. It is perhaps because of this diversity in form, function and habitat that there have been relatively few authoritative textbooks treating them.

Bone and Marshall have produced just this. Following a brief account of the diversity of fishes, giving details of the features of each major group, they provide analysis of the basic biology of fishes. Chapters dealing with swimming, buoyancy, osmoregulation, gas exchange and circulation, and reproduction, approach each topic from an anatomical stance with broad discussion of the physiological processes involved. The final chapters on sensory systems and the central nervous system contain stimulating discussions on aspects of these systems, making full use of the latest literature while also serving as a vehicle for the authors' own researches.

According to the preface, the book is designed for advanced undergraduates and postgraduates but the authors assume a very considerable foundation in natural

breathlessness and one doubts whether the book is quite as "intelligible to the uninitiated as to the well informed" as is claimed in the preface. However, Calow does succeed in communicating the excitement of a developing field. His book might best be read after working through Ayala's more sedate treatment of the subject.

Although each of these books is in its own way a success, neither is a new approach to the problem of synthesis in evolutionary biology. The recent evolution of textbooks on evolution has been, like evolution itself, a gradual process. Not for many years has there been a macromutation such as those which produced Fisher's *Genetical Theory of Natural Selection*, or Goldschmidt's *Major Features of Evolution*. The world still awaits a convincing synthetic treatment of modern views on the subject. □

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sciences on the reader's part. I would suggest that only exceptional undergraduates would be able to understand it throughout, but many specialists will find it of outstanding value for the summation of the literature and the insights into fish biology provided.

In *Fishes* Moyle and Cech have aimed for a wider readership although primarily addressing students of fish biology. Their treatment of the orders of fishes is extensive and includes discussion of the major families, the reader gaining a wider perspective as a result. The authors also dwell on ecology rather than purely descriptive morphology which has the effect of producing a text about living creatures not specimens. An introductory section on structure and form, which includes accounts of morphology, respiration, feeding, reproduction, sensory perception, and behaviour and communication amongst other topics, provides background information of the classical kind. Later parts of the book on zoogeography and ecology combine to produce a complete account of the natural history of fishes.

Moyle and Cech have produced a refreshingly new, general account of ichthyology. Their book deserves to take its place as a textbook on ichthyology for undergraduate students, and will serve to broaden the horizons of many others whose work or hobby brings them into contact with fishes.

These two books are not competitors but are properly complementary. Moyle and Cech provide a broad background to ichthyology; Bone and Marshall take the subject deep into the fields of anatomy and physiology. Together they mark a great advance in the presentation of our knowledge of fishes. □

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Mechanisms in the balance

Thomas E. McGill

Ethology. By James L. Gould.
W. W. Norton: 1982. Pp. 600.
\$22.95, £12.25.

Biology of Behaviour.
By Donald M. Broom.
Cambridge University Press: 1982.
Pp. 316. Hbk £22.50, \$39.95;
pbk £8.95, \$14.95.

IN HIS highly influential paper, "On Aims and Methods of Ethology" (*Z. Tierpsychologie* 20, 410–433; 1963), Niko Tinbergen listed the four basic types of questions posed in the study of animal behaviour: causation, development, evolution and function (survival value). Dozens of general textbooks dealing with animal behaviour have been published in the 20 years since that article appeared, differing greatly in the emphasis placed on the questions posed by Professor Tinbergen. The pendulum has, of course, swung erratically, but most recent authors have stressed the questions of evolution and survival value over that of mechanism.

The two books reviewed here represent a redress of the balance. Indeed, this shift is indicated in the subtitles the authors have selected — *The Mechanisms and Evolution of Behavior* (Gould) and *Mechanisms, Functions and Applications* (Broom). In that sense, the two books are similar and equally welcome. But there are notable differences in the approaches the authors have taken to their subject.

One of Gould's purposes is to demonstrate that E.O. Wilson was wrong when he predicted in *Sociobiology* that ethology would split into two different camps, one with a strictly mechanistic approach and the other posing evolutionary questions. Gould attempts, with a good degree of success, to intermingle both viewpoints.

He begins with some interesting, pedagogically useful, chapters on the history and development of modern ethology. He then proceeds to build his animal from the inside out, considering first neural mechanisms and sensory processes. Part III, entitled "Complex Behavior", includes excellent chapters on orientation, navigation and communication. After a section on learning, there are two brief chapters on behavioural genetics describing such familiar examples as Dilger's lovebirds, Tryon's rats and Rothenbuhler's bees. The final sections cover evolutionary mechanisms, social behaviour and human ethology. The section on social behaviour consists of five chapters each of which is concerned with a particular group of animals — e.g. honey bees, African ungulates and African carnivores — but a major omission is the lack of any description of those species

whose social structure most closely parallels that of early man; the wolves.

Each of the chapters in *Ethology* is followed by a list of carefully thought-out study questions that should prove useful to both student and instructor.

Broom's approach to the subject is quite different. He does not organize his text into parts, instead presenting ten chapters covering such topics as the allocation of resources, body regulation and maintenance, feeding and antipredator behaviour. Like Gould, he begins with sensory and motor processes and ends with group behaviour.

As his subtitle and some of his chapter titles indicate, Broom is concerned with the practical applications of animal behaviour studies. His book starts with a page called "The Behaviour of Farm Animals and Pests" which presents a list of 35 topics and the chapter and page where discussion of each topic will be found — for example, "Defence responses by farm animals to

man" refers to a discussion in the antipredator chapter indicating that the behaviour of the cowman can affect milk-yield and that particular behaviours on the part of the farmer can reduce the chances of "hysterical" reactions in bird flocks; and "Responses to poisons: locusts, rats" discusses, among other things, the work of Garcia's group on learned taste aversions.

In part because of its applied flavour, Broom's book is quite different from any other text in animal behaviour that I have encountered. I doubt that many instructors of the usual college or university course in animal behaviour would make the book their first choice. It may, however, prove useful to teachers of veterinary or agriculturally-orientated programmes. □

Thomas E. McGill is Hales Professor of Psychology at Williams College, Williamstown, Massachusetts. He is editor of *Readings in Animal Behavior* (Holt, Rinehart & Winston), now in its third edition.

Insects explained

M.E.G. Evans

The Insects: Structure and Function,
3rd Edn.

By R. F. Chapman.
Hodder & Stoughton/Harvard University
Press: 1982. Pp. 832. £19.50, \$35.

THE INTRODUCTION to *Nature's* 1982 textbook supplement emphasized that the most warmly welcomed textbooks are new editions of standard works. This third edition of a book which rapidly is becoming an entomological classic is a particularly good example.

The Insects deals with how insects work rather than how they are classified, and it uses a whole-animal approach, including behavioural and ecological details. Chapters describing the structure and functions of the head, thorax and abdomen are each used to introduce a series of related physiological chapters. A high standard of illustration is seen in the many large, clear line drawings with their simple block shading and unabbreviated labels; all have been redrawn, rather than copied, in the same effective and economical style. The third edition has grown by over 70 figures and an extra 100 pages in an attempt to include the most important work of the past decade. The new material has been integrated into the appropriate sections of each chapter, and the references are now quoted chapter by chapter rather than at the end of the book.

This book is aimed at advanced undergraduate students, and I think that it would provide a very suitable background text for an MSc course. It is as large as many multi-author volumes, but it has the coherence and lucidity characteristic of the best single-author works. Of course, this may

also produce a personal view of some controversial topics, and there are a few sections where less orthodox viewpoints might have been included: for instance, Dennell's model of the cuticle, or Baker's interpretation of migration. However, Chapman presents a well-balanced selection of work relevant to most entomology courses.

V.B. Wigglesworth considered the first edition of *The Insects* to be "a really useful book"; this was a particularly generous appraisal since his own classic text *The Principles of Insect Physiology* (Chapman & Hall, 7th Edn 1972) is one of its closest competitors. This latest revision of *The Insects* enhances the usefulness of Chapman's text and establishes it as one of the best available. □

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One type of textbook

Alan E.H. Emery

Genetics. By George P. Rédei.
Macmillan/Collier Macmillan: 1982.
Pp. 720. \$27.95, £15.95.

THE subject of genetics now embraces so much that it is doubtful if any one textbook can ever cover the entire subject in any detail. Yet authors remain undaunted by this formidable task. Not all have been equally successful though there have been some notable jewels, for example I.H. Herskowitz's *Principles of Genetics* (Macmillan/Collier Macmillan, 2nd Edn 1977). The other problem facing the writer of an undergraduate textbook of genetics is defining the way in which it will be used. Should it be a strictly didactic text,

complete in itself with questions and answers? Many North American writers obviously prefer this approach. Alternatively should the author rely more on the instructor and concentrate on the principles of the subject? This approach is perhaps more favoured in Europe.

Rédei's textbook falls into the first category and is meant to provide a general introduction to the subject for undergraduate courses. The main emphasis is on cytogenetics, molecular genetics and population genetics. Biochemical aspects of the subject are dealt with wherever indicated, but there is no specific section devoted to this. Examples are chosen from the whole range of living organisms, I suppose to emphasize the holistic nature of the subject. However, I suspect that on occasions the student may well be confused by the close juxtaposition of information on widely disparate organisms. Intersex in asparagus and pig, for example, appear in the same illustration.

Apart from covering the principles of the subject, the author also provides a welter of detail which may sometimes do no more than discourage even the most diligent student. For example, the precise locations of some 200 loci in the human genome are given. Many students may legitimately ask how much of this sort of information they need to know and remember.

The strength of *Genetics*, however, lies in the sections dealing with molecular

genetics which are remarkably clear and up to date, including for example discussions of oncogenes and the transfection assay. The book is extremely well illustrated with countless clear line-drawings. Each chapter concludes with a well-chosen bibliography and problems, answers to which are provided. There is an excellent glossary and

also a detailed index. Of its type, this is one of the best textbooks of general genetics, though the student will require careful guidance in selecting out what is particularly relevant to him. □

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Practical distillate

J.M. Grainger

Sourcebook of Experiments for the Teaching of Microbiology.

Edited by S.B. Primrose and A.C. Wardlaw.

Academic: 1982. Pp. 766. £28.80, \$53.50.

A FEW YEARS ago the Society for General Microbiology Teaching Group discussed the idea of sharing stimulating and reliable experiments from undergraduate classes with those of colleagues from other institutions. This project has now come to fruition in the form of an absorbing and unusual book, one of the Special Publications of the Society.

The book is a distillate of less than 10 per cent of a vast amount of material collected together by the editors, mainly from within the United Kingdom. The 111 experiments are grouped into nine somewhat unconventional sections and include illustrations of growth and death; biochemistry and genetics; relations of microorganisms with soil, water, plants and animals; and industrial microbiology. The editors were limited in their aim of having fair representation of prokaryotes and eukaryotes and the viruses by inevitable deficiencies in the material offered; thus 60 per cent of the experiments involve bacteria. A few experiments entail the use of microorganisms (and procedures) that some might consider potentially hazardous, a judgement which the editors intentionally leave to the reader.

Each experiment is presented in a common format: Information panel (level, subject area, special features); Introduction (background, objectives); Experimental (flow diagram, time taken); Materials (special requirements for teacher and technician); Specific requirements (complete list, day by day); and Further information (sample results and their interpretation, references, suggested extensions to the experiment). Basic procedures such as Gram's stain and use of the microscope are omitted because the book is intended for teachers not students, and as an extension to existing basic teaching manuals.

Undergraduate classes in practical microbiology now should be less dull if the hopes of the editors are realized; particularly, one would think, in some of the institutions not represented in the book! However, there remains a great need for suitable material to help the promotion of microbiology in schools. This is another

matter to which the Society for General Microbiology is giving particular attention through its support of MISAC, the Microbiology in Schools Advisory Committee. □

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Viral displacement

Alison Newton

Virology.

By Heinz Fraenkel-Conrat and Paul C. Kimball.

Prentice-Hall: 1982. Pp. 400. \$38.20, £30.55.

STUDENTS of all branches of biology, from ecology to molecular genetics, need to understand the essentials of virology. Since 1953 successive editions of Luria *et al.*'s *General Virology* (Wiley, 3rd Edn 1978) have served to introduce many generations of students to the subject, but even the latest edition of this splendid textbook is now, sadly, too old to cover many aspects of viral replication. An up-to-date textbook that makes few assumptions about background knowledge would therefore be welcome.

The publication of *Virology*, whose senior author, as editor of a marathon series on virology, should be in an excellent position to cover all aspects of viruses, raised hopes that a replacement for *General Virology* had been found. Unfortunately *Virology* falls far short of the standards set by Luria and his colleagues. Although containing detailed accounts of the latest schemes for replication of most viral nucleic acids and proteins, and recent information on uses of viruses in genetic manipulation, the book fails to provide a balanced view of the nature of viruses. It caters more for the biochemist than for the natural historian or pathologist.

Somewhat surprisingly, since arrangement of the book is based on a discussion of strategies of viral replication classified according to the scheme proposed by Baltimore for synthesis of messenger RNA, there is no general discussion of that scheme. Furthermore, classification of all plant viruses is included under the heading "Unenveloped plus-strand viruses" and, even more confusingly, classification of both RNA- and DNA-containing animal

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viruses is described in the chapter on enveloped plus-strand viruses. This does not help the student to disentangle the complex problems of viral classification. Although an advantage is that more attention is given to plant viruses than is generally the case, it is nevertheless disappointing to find that only two pages out of four chapters on virus-cell interactions are devoted to plant pathology.

The authors have adopted a complicated system of emphasis of key words that personally I find so distracting as to be self-defeating. One wonders for instance why "virion proteins", "the nature of life" and "animal virologists" should appear in italics whereas "capsomers" and "professional virologists" merit bold type. Moreover, the general standard of presentation of diagrams and photographs is lower than we have come to expect in standard textbooks. For all these reasons I shall continue to advise my students to buy one of several recent paperbacks for details of virus replication and to return to older textbooks to gain a general understanding of the subject. □

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Quantity and quality in the study of microbial ecology

J.H. Slater

Environmental Microbiology.

By W.D. Grant and P.E. Long.

Blackie/Halsted: 1982. Pp.212.

Hbk £17.50, \$27.95; pbk £8.50.

Microbial Ecology: Fundamentals and Applications.

By Ronald M. Atlas and Richard Bartha.

Addison-Wesley: 1982. Pp.560.

\$28.95, £13.50.

SEVERAL influential textbooks on microbial ecology appeared about 15 years ago and have remained largely unchallenged as basic texts for degree level courses. Although in a less spectacular fashion than molecular biology and microbial genetics, microbial ecology has progressed rapidly during the intervening period; it has moved through a qualitative, "natural history" phase to become a more quantitative science which incorporates a substantial body of information derived from microbial physiology, biochemistry and genetics.

Both of the present books reflect this shift in emphasis and will be adopted as the next generation of undergraduate texts — indeed they are already widely accepted and used. They are worthy successors to the earlier efforts to present microbial

ecology as a valid branch of modern microbiology.

The two books have been written with senior undergraduates in mind and are both well presented. In places they might be considered simplistic by such students, especially those who have been fed on a good basic diet of physiology and biochemistry. *Microbial Ecology* in particular contains introductory material which will be found in general microbiology texts. On the other hand such an approach rightly demonstrates the need to base ecological studies on sound principles, and in this respect *Environmental Microbiology* is limited. Each, regrettably, excludes any serious, in-depth appraisal of genetic processes in an ecological context.

Grant and Long's offering is much the smaller of the two books, containing potted (but well potted) descriptions of major habitats, the important elemental cycles and microbial activity in pollution problems. It is a thoroughly readable text, written with an economy of style which gives a good ratio of fact to page size. *Environmental Microbiology* has the characteristics to supplant previous texts occupying the small-book niche of the market: it is, however, not a substantial competitor to *Microbial Ecology*.

Atlas and Bartha have produced an impressive book. A welcome feature is the careful balance that has been maintained between accounts of the major standpoints in modern microbial ecology: habitat description has not been overweighted compared to, say, a biogeochemical cycle approach. The crucial areas of experimental design, data analysis and modelling (often neglected and badly taught) are necessarily highlighted and the procedures are usefully described in an ecological context. The importance of understanding ecological principles as a prerequisite to exploiting environmental processes is acknowledged. Finally a good collection of well-selected review and primary articles provides a springboard to further study.

Although their intended clients are the same, the books will appeal to decidedly different groups. It is invidious to select one or other of these useful texts, but a split decision goes to Atlas and Bartha with a generous round of applause for the runner-up. □

J.H. Slater is Professor of Applied Microbiology at the University of Wales Institute of Science and Technology, Cardiff.

Textbook supplement — prices

Where appropriate, both dollar prices pertaining in the United States and sterling prices for the United Kingdom are given in the bibliographical details for each book. Export prices will generally be higher. If a dollar or sterling price is not cited, the book is not available in one of the two countries. However readers should check both price and availability of books before ordering.

An index to all of the books reviewed in this issue appears on pp.192-193.

Mega microbiology

R. Whittenbury

Microbiology: An Introduction.

By Gerald J. Tortora, Berdall R. Funke and Christine L. Case.

Benjamin/Cummings: 1982. Pp.770.

\$28.95, £20.25.

The Microbial Perspective.

By Eugene W. Nester *et al.*

Saunders: 1982. Pp.730. \$43.45, £21.95.

Biochemistry of Bacterial Growth, 3rd Edn.

Edited by Joel Mandelstam, Kenneth

McQuillen and Ian Dawes.

Blackwell Scientific/Halsted: 1982.

Pp.450. Hbk £28; pbk £15.50, \$34.95.

Introduction to Bacteria for Students in the Biological Sciences.

By Paul Singleton and Diana Sainsbury.

Wiley: 1982. Pp.167. Hbk £11, \$31; pbk

£4.95, \$13.95.

PEDAGOGY and publishing technology seem to be the American answers to the problem of how to present microbiology of yesteryear in an elementary fashion to the college students of today. Superb illustrations (often in colour), short factual inserts and graphics of high quality all add to the coffee table splendour of these products. But their real educational value remains a mystery. This poses the rhetorical questions — do students really appreciate or need all this effort, or would they prefer some old-fashioned freedom of action to exercise their intelligence?

Microbiology: An Introduction and *The Microbial Perspective* are good examples of this particular genre. Both are aimed at students with no chemistry background of consequence and little or no previous knowledge of biology. Both texts are supposed to be introductions to microbiology, but their contents don't really support this broad claim. Each is heavily orientated towards medical microbiology, and, of the types of student for which it is claimed they have been produced, it is clearly the "allied-health sciences" group which is the real target. In that context both textbooks seem to be successful as pieces of total teaching technology, if not as literary gems.

Every now and again masochism is rewarded — and against all odds the cynical reviewer of microbiology textbooks is forced to resort to fulsome praise to ensure that students take note and are stimulated to rush out and purchase the book in question. *Biochemistry of Bacterial Growth* is a textbook in this category. Now in its third edition, it is beginning to provide both the breadth of cover and depth of treatment required by today's microbiology undergraduates — and potential biotechnologists. The improvement is not in the writing or presentation, consistently of a high standard in all editions, but in the subject area embraced. For once, the title is an accurate description

of the contents. And, paying due deference to the slight sensitivity of the editors to criticism (see preface), a fervent hope is that this trend will be maintained in subsequent editions. To pluck just two examples out of the mud, dinitrogen fixation and one-carbon metabolism are topics which merit the detailed attention of the editors in future. Both provide instances of important metabolic principles — and both are subjects of importance in the comprehension of the biochemistry of bacterial growth.

The book is a compilation of chapters written by different authors, but for once it is not a discordant collection of writings; the editors have exercised considerable skill in maintaining the interest of the reader.

The book starts with a chapter on the anatomy of the bacterium and proceeds via the mechanism of synthesis and provision of building blocks and relevant genetics to the very important, but frequently neglected, subject of differentiation. The most recently recruited editor, Ian Dawes, makes a creditable first stab at this last topic, enough to encourage *aficionados* in their expectations that the treatment will be further expanded in the next edition. A very useful appendix, or miscellany, winds up the treatise — particularly useful is the taxonomic summary.

A final comment is reserved for the organization of the book, a mild foray into pedagogy which might prove successful. A bird's eye view of the contents (an abstract) leads to an abbreviated version (highlighting the principles) so permitting the following very full treatment which does not have to be continually interpreted (spoiled) by signals to the student. This is an excellent text to be recommended to all microbiologists, not just students.

The last book, *Introduction to Bacteria*, is a first venture of distinct promise designed for students of biology who require slightly more than a nodding acquaintance with microbiology. It will also serve as a useful survey of the subject for students contemplating specialization in microbiology. A few minor irritations jar a little — for example, milk sugar can be safely revealed to be lactose in the next edition; the very artificial separation of cyanobacteria from all other bacteria is not merited (i.e. some species can photosynthesize anaerobically using hydrogen sulphide as an electron donor); and neither meiosis nor mitosis are mechanisms of cell separation.

These sorts of peccadillos aside, this is a well-conceived text written by authors who clearly have a very good insight into recent literature (i.e. their prejudices coincide with those of the reviewer). One could quibble with the brevity of treatment in some instances but, all in all, *Introduction to Bacteria* is a welcome addition to the fold. □

R. Whittenbury is Professor of Biological Sciences at The University of Warwick.

Quart in a pint pot

D.D. Davies

Plant Cell Structure and Metabolism, 2nd Edn.

By J.L. Hall, T.J. Flowers and R.M. Roberts. Pp.539. Longman: 1982. £12.95, \$22.

THE recently completed series *A Comprehensive Treatise on Plant Biochemistry*, edited by P.K. Stumpf and E.E. Conn, has the laudable object of reviewing all the aspects of plant biochemistry. That series, however, consists of eight volumes at a cost which restricts its purchase to libraries. This second edition of *Plant Cell Structure and Metabolism* makes a valiant attempt to keep up with recent advances and additionally to relate biochemistry to the structural organization of cells, illustrated by 90 electron micrographs. The authors' admirable effort is achieved with a 27 per cent increase in size over the first edition, but the book still comes at a price which students can afford.

The distillation of wine to produce brandy can be achieved with little loss of alcohol, but the concentration of biochemistry and cell physiology into a

single volume requires the elimination of many important topics. Individual readers will check to see if their selection accords with that made by the authors.

My prejudice is that the failure to discuss plant hormones is a mistake. I found the discussion of metabolic control inadequate and that of the control of glycolysis erroneous, as well as being out-dated. I would in particular take issue with the authors' claim that "Chapter 2 gives a sufficient background of cell chemistry for the book to be read without the aid of other biochemical texts". Students should be encouraged to increase their understanding of chemistry and not lulled into a false sense of security by a mere 87 pages on the subject. Moreover, the teaching of chemistry in schools has changed, so that students will know the structure of ethanoic acid but not that of acetic acid! A new book should recognize changes in nomenclature.

These adverse comments must be seen against the overall excellence of the book. It is a worthy modern biochemical equivalent to Haberlandt's classic *Physiological Plant Anatomy* and should be owned by every serious student of botany. □

D.D. Davies is a Professor in the School of Biological Sciences, University of East Anglia.

Pathology for the botanist

R.K.S. Wood

Virology of Flowering Plants.

By W.A. Stevens. Blackie/Chapman & Hall: 1983. Pp.182. Hbk £17.50, \$39.95; pbk £8.50, \$18.95.

Plant Pathology and Plant Pathogens, 2nd Edn.

By C.H. Dickinson and J.A. Lucas. Blackwell Scientific/Halsted: 1982. Pp.230. £7.80, \$17.95.

Principles of Plant Pathology.

By J.G. Manners. Cambridge University Press: 1982. Pp.264. Hbk £22.50, \$47.50; pbk £8.95, \$17.95.

PLANT pathology has long had a prominent role in the teaching of agricultural sciences. But only relatively recently has it also become important in the teaching of plant sciences — including much of microbiology — and it will become more so with the expansion of technologies based on plant sciences. Because of past neglect, however, there are still not all that many books on plant pathology and fewer still on plant viruses at levels taught to undergraduates in Britain and presumably elsewhere. The three books reviewed here are intended to serve these levels.

Stevens's *Virology of Flowering Plants*

has a good introductory chapter, apart perhaps from the undue emphasis on cryptograms which is out of place. The second chapter on symptoms has a good text and diagrams but the photographs of symptoms are mostly poor, a pity because symptoms of virus diseases are often so eye-catching. Chapter 3 on transmission of viruses to plants is efficiently comprehensive for a book of this size — the diagrams again being much more useful than the photographs — and the following two chapters, on structure and on replication, are well illustrated with a clear text despite the complexities which may be somewhat beyond the needs of most undergraduates.

The control of the diseases is well summarized in the penultimate chapter, and the book ends somewhat surprisingly but refreshingly with an account of techniques — but would this chapter not be better placed after the Introduction? The bibliography of some 300 references is long and divided according to chapters. Only students can tell how useful this is, but they are likely to be well satisfied with the rest of the book as a clear and comprehensive introduction to the subject.

The other two books, both dealing with plant pathology, are very different in style and content from *Virology of Flowering Plants* in being more about principles and based less on detail. Viruses are included by both Dickinson and Lucas, and Manners, but there is not much about them compared with microorganisms.

Plant Pathology and Plant Pathogens is a second edition of a book published in 1977. It is essentially similar to its predecessor, but brought up to date and with a number of minor improvements (longer and better reading lists at the end of each chapter to a total of some 100 references, and an expanded and greatly improved Chapter 9 now renamed "Host-Pathogen Specificity"). The book deals successively with microbial pathogens, their structure and function, infection and colonization, diseases in populations and at the whole plant, cellular and molecular levels, with specificity and with disease control. It is well illustrated, the 90 or so figures being simple yet informative, and the text is clear

and interesting. The book is a useful survey of the general features of diseases caused by microorganisms and will be attractive to students; it would, however, be improved by some reorganization of the contents of the three chapters dealing with the diseased plant and with pathogens.

Manners's *Principles of Plant Pathology* covers the same ground but is quite different in content and presentation. There are five parts, successively on causes, physiology, genetics, epidemiology and control of plant diseases. This is a straightforward, well tried and probably the best sequence. Each part is divided into sections, the order of which is again logical, and the text is well written and easy to

absorb. There are no more than 36 diagrams and photographs, and 14 tables; quite a few of each are not so illustrative as they should be to balance the general quality of the text. There is a very useful glossary, but while the list of some 600 references may suit teachers, students will find it formidable. This again is an attractive book, and I would hesitate to recommend to a student which of the two books on plant pathology to buy if only one of them can be. □

R.K.S. Wood is Professor of Plant Pathology and Head of the Department of Pure and Applied Biology at Imperial College, University of London.

Forms and functions in the plant sciences

James F. Sutcliffe

Plant Anatomy, 3rd Edn.

By A. Fahn.

Pergamon: 1982. Pp.544.

Hbk £30, \$60;

pbk £13.50, \$27.

Agricultural Plants.

By R.H.M. Langer and G.D. Hill.

Cambridge University Press: 1982.

Pp.343. Hbk £20, \$39.95; pbk £7.95, \$15.95.

Plant Growth Substances Including Applications in Agriculture.

By H.N. Krishnamoorthy.

Tata McGraw-Hill: 1982. Pp.214. £7.75, \$12.50.

ALTHOUGH anatomy does not feature prominently nowadays in botanical teaching, a sound knowledge of plant structure is still important. Anyone brought up on Professor Esau's splendid *Plant Anatomy* and *Anatomy of Seed Plants* may wonder whether an alternative textbook is needed. The fact that Professor Fahn's book is now in its third edition supplies the answer. The text of the book — originally translated from Hebrew by Sybil Broido-Altman — is clear and concise, and covers the development of structures as well as providing accurate descriptions of mature tissues. One is not overwhelmed by botanical terms, the most important of which are found in a useful glossary. There is an up-to-date list of key references to research and review papers at the end of each chapter, and extensive subject and author indexes are also included.

The 21 chapters are divided into four main groups covering mature tissues, the primary and secondary vegetative bodies, and reproductive organs. Attention is given mainly to angiosperms and, apart from a description of gymnosperm wood, other plants receive scant attention. The

text is well-illustrated by numerous line drawings and photographs including some excellent recent scanning electron micrographs.

There is a brief introduction to plant anatomy as a prelude to Langer and Hill's *Agricultural Plants*, but the book consists mainly of some 300 pen-portraits of plants used in agriculture. It deals with their history, cultivation and uses as well with some more botanical aspects. There are pleasing and accurate line drawings to aid identification and to illustrate features of special interest. The book is confined mainly to temperate crops; tree species and plants of predominantly horticultural interest are excluded.

The plants are arranged in families starting with monocots. More than half the book is taken up with descriptions of members of the Gramineae and Leguminosae while some families — the Malvaceae and Papaveraceae, for example — are represented by only a single genus. A final chapter, which seems to be rather out of place, deals briefly and somewhat superficially with the physiological basis of yield; among the topics covered are plant development, crop photosynthesis and the distribution of dry matter. The reader will search in vain for any information about the role of growth regulating substances in these processes, although the gibberellins are mentioned briefly earlier in the book in connection with the germination of cereal grains and malting of barley.

This deficiency is remedied by H.N. Krishnamoorthy in *Plant Growth Substances*. The treatment, however, is unexciting. Each of the groups of growth regulators — auxins, gibberellins, cytokinins, abscisic acid, ethylene and retardants — is dealt with systematically in a separate chapter covering discovery, history, extraction, assay, biosynthesis, physiological effects and mode of action. While this approach has its merits, particularly for the student who likes to have information cut and dried, it suffers from the disadvantage that interactions between different growth regulators tend to be overlooked. To discover the integrated role of the various groups of substances in a par-

ticular process, for example flowering, requires a good deal of effort even with the help of the subject index.

The standard of production of *Plant Growth Substances* compares unfavourably with the other two books reviewed here. No doubt the resultant saving in cost will be welcome to students, not only in the Third World, but the lack of photographs and the poor quality of the line-drawings detract seriously from the book's attractiveness as a student text. □

James F. Sutcliffe has retired recently as Professor of Plant Physiology at the University of Sussex.

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Striking the autecological balance in plant ecology

Peter D. Moore

Introduction to Plant Population Ecology.

By Jonathan W. Silvertown.

Longman: 1982. Pp.209. £7.95, \$17.95.

Environment and Plant Ecology, 2nd Edn.

By J. R. Etherington.

Wiley: 1982. Pp.487. Hbk £25, \$59.95; pbk £12, \$28.

Ecology of Woodland Processes.

By John R. Packham and David J. L. Harding.

Edward Arnold: 1982. Pp.260. £8.95, \$19.95

IF THERE is one area of plant ecology which can truly be said to be blooming, it is the study of population ecology. After decades of emphasis on the synthetic, or community approach to ecology, the analytic, autecological balance is now being struck. Undoubtedly the publication of John Harper's *Population Biology of Plants* (Academic, 1977) has been a strong, stimulating factor in this development at the research level and its recent issue as a paperback has brought it (financially speaking) within the reach of undergraduates. But Jonathan Silvertown has now made a brave attempt to produce an introductory text on this subject, aimed directly at the undergraduate.

The book is briefer than Harper's, more visual in its approach (undoubtedly a product of the author's teaching experience at the Open University), uses a simpler style and, in general, assumes less background knowledge in the reader. But it is certainly not an oversimplified book. The need for a numerical approach and the value of mathematical modelling (including matrix-based models for populations with an age structure) is emphasized even in the first chapter. Beginning with life tables, seed dormancy and the seed bank, the author works his way through recruitment, demography, reproductive strategies, self-thinning and vegetative propagation. In all of these topics he draws liberally upon recently published experimental data which serves to underline the rapid advance of the subject.

In his final two chapters Silvertown tackles species interaction, competition and the concept of the niche. Again, as each concept or topic is introduced it is clearly illustrated by reference to an appropriate example from the literature. This leads to a lively development of the text and is a credit to its author's familiarity with the literature. It will make this book an excellent tool for the introduction of plant population biology to undergraduates and will also serve to open a wealth of valuable literature to postgraduates entering this field.

Etherington's *Environment and Plant Ecology* has already earned a respected position among undergraduate texts along-

side Bannister's *Introduction to Physiological Plant Ecology* (Blackwell Scientific, 1976) and Larcher's *Physiological Plant Ecology* (Springer-Verlag, 2nd Edn 1980). Etherington has now considerably revised and expanded the book in a number of areas. Radiation balance and microclimate are dealt with in far greater detail, while the soils' section has been subjected to a rather less extensive revision but has been brought up to date in its literature coverage. A good balance is still maintained between topics such as soil profile description and geographical variation within soils, and the physico-chemical soil environment within which plant roots develop. The coverage of soil is generally stronger here than in competing books.

The response of the plant to radiant energy is a portion of the book which has changed beyond recognition. The lack of emphasis in the first edition on the light climate and photosynthetic pathways has now been thoroughly rectified, though the consideration of the ecological implications of the C_4 photosynthetic pathway could well have been developed further still, even though it is touched upon again in the chapter on water stress. A new chapter on climate and plant response has been inserted, which also refers back to the C_4 theme, as well as covering such topics as frost hardiness, seed germination and day-length responses.

The revisions, overall, are thorough and worthwhile, and the book has improved considerably since the first edition. It is assured of retaining an important position in this competitive field.

Books concerned with specific habitats must, by their very nature, have a more limited sales potential as undergraduate texts. Few courses are run on a habitat basis, but many concentrate upon particular habitats, particularly from the point of view of field work. The habitat-based book may, therefore, have its undergraduate appeal. Packham and Harding's *Ecology of Woodland Processes* is an ambitious attempt to introduce a spatially and biologically complex habitat at this level and to use the opportunity to expose the student to a variety of modern ecological concepts. Unfortunately, it is the first

chapter, the "Introduction", which is the least successful. The authors try to pack far too many ideas into the first few pages, with the result that the reader is swept through population structure, allelopathy, hydrological cycles, production and r - K selection in the space of 20 pages. Many of these subjects are returned to later but this is enough to leave the beginner with mental indigestion, from which he is unlikely to recover. This tendency to skate over subjects superficially persists throughout the book. New terms (in heavy print) are introduced at a prodigious density, often as high as seven or more to the page. This could be tolerated if the terms were adequately defined, but sadly this is not always the case.

There are some features in this book which deserve considerable praise, such as the varied and interesting assortment of examples quoted to illustrate ecological points, many derived from non-British data, which is refreshing. It is also pleasing to find a cooperative venture between a botanist and a zoologist, though integration could have been more extensive. The book is weakened simply by trying to cover too much ground in too little space. □

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On the safe side of pesticides

G.R. Sagar

Herbicides and Plant Growth Regulators.

By W.W. Fletcher and R.C. Kirkwood.

Granada, St Albans, Herts/Renouf,

Brookfield, Vermont: 1982.

Pp.408. £25, \$61.25.

The Chemistry of Pesticides: Their Metabolism, Mode of Action and Uses in Crop Protection.

By Kenneth A. Hassall.

Macmillan, London: 1982. Pp.372.

Hbk £30, \$46.20;

pbk £15, \$23.10.

PESTICIDES are an emotive subject and very big business economically. They are also a real problem when trying to write a comprehensive textbook, not least because of the fascinatingly interdisciplinary nature of the subject.

In *Herbicides: Physiology, Biochemistry, Ecology* (Academic, 1976), Professor Audus solved the difficulty by inviting many authors to contribute articles on their specialisms; the risk with this approach is that integration of the various topics is reduced. In their attempt to provide all-embracing coverage of herbicides, W.W. Fletcher and R.C. Kirkwood run into a different problem — there are so many

herbicides — and the reviews have become catalogues. Nonetheless such a book has value as a work of reference and *Herbicides and Plant Growth Regulators* does contain a significant amount of material on general principles and issues.

In *The Chemistry of Pesticides* Kenneth Hassall dodges these problems because his book is less comprehensive — despite the publisher's claim — and thus much more readable. It goes beyond its main title but demands a high standard of background chemistry on the part of the reader. Clearly, there is overlap on herbicides between the two books, but little disagreement in interpretation appears.

The inclusion by Fletcher and Kirkwood of plant growth regulators as bedfellows with herbicides has the logic of the common origin of these materials in the chemical industry and the fact that herbicides have to interfere with some aspect of growth to be effective. The introduction of allelopathy into the discussion should have provided an opportunity for a critical appraisal of this contentious subject. Unfortunately the opportunity was not taken; instead there is the bland repetition of various claims to be found in the literature, some of the text being no more than a thinly-disguised abstract of the summaries of published papers. Readers of this section would be well advised to refer to L. G. Stowe's article in the *Journal of Ecology* (67, 1065; 1979) which exposed the fragility of the methods used to "display" allelopathy.

It would, however, be unfair to level the charge of missed opportunities at the one book — both deserve it, for both are ever-so-safe in their approach. Neither challenges published claims except when two studies have yielded different answers; even then, attention is usually drawn only to the discrepancy. Nor in either book is there a real attempt to look forward or to expose our ignorance. Reading between the lines it becomes pathetically clear how little we know of the relevant anatomy and physiology of plants — how do pesticides penetrate into leaves and how are they taken up by roots; what is the structure of the foliar pathway; how do foliage-applied translocated herbicides get into the phloem; what are the mechanisms of selectivity? On the other hand both books do reflect our considerable understanding of the biochemistry of pesticides once they get into cells.

Despite their failings these two books ought to find their way on to library shelves in that they update earlier, comparable volumes. The authors can presumably recommend them to their own students and, not having to teach the subject, can develop new courses in those areas vacated by their prematurely-retired colleagues. Come to think of it, I could do that too! □

G.R. Sagar is Professor of Agricultural Botany at the University College of North Wales, Bangor.

On time but out of rhyme

M.D. Lilly

Principles of Biotechnology.

Edited by Alan Wiseman.

Surrey University Press/Methuen: 1982.

Pp.192. Hbk £10.95;

pbk £8.95, \$23.95.

THE recent rediscovery of biotechnology, partly triggered by the development of recombinant DNA techniques, has led to a flurry of activity in Britain and elsewhere. In particular there has been much debate about the teaching of biotechnology and the training of biotechnologists.

Although the Royal Society Report on Biotechnology and Education published in 1981 deprecated undergraduate degrees in biotechnology, it advocated that undergraduates in the biological sciences and chemical engineering should be made aware of the ways in which their disciplines contribute to biotechnology and particularly industrial biological processing. Thus there is a need for a few high-quality textbooks on biotechnology, and it was with interest that I opened this book. I regret to say that I found it disappointing for several reasons.

First, the overall standard of presentation is poor. It is a pity that more effort was not made to proof-read the book because it contains many serious errors, both typographical and factual. Several important equations, for instance those for protein release and protein precipitation, and chemical structures are wrong — the structure shown for streptomycin is actually that of glucose. The chapter on inter-relationships in biotechnology referred to on the back cover has been omitted.

Secondly, the book contains a large number of naive or incorrect statements which is most worrying as a non-biotechnologist reading the book is likely to be badly misled. I am well aware of the problems of compiling a multi-author book but feel that more coordination between the authors would have been beneficial. There are several cases of repetition or, worse, of conflict of information.

No single volume can cover all aspects of biotechnology and this book concentrates on fermentation and enzyme technology. It starts with a chapter on features of biotechnology and its scientific basis, followed by four chapters on the application to biotechnology of the principles of industrial microbiology, microbial genetics, fermentation engineering and enzymology respectively. The last two chapters describe the biotechnology of enzyme isolation and purification, and the application of immobilized enzymes, immobilized cells and biochemical reactors in biotechnology.

I cannot recommend *Principles of Biotechnology* and will positively

discourage its use by my students; it is certainly not "the perfect introduction" the cover blurb declares it to be. I get the impression that it has been rushed into print and I strongly urge the publishers to revise the book at the earliest possible opportunity. □

M.D. Lilly is Professor of Biochemical Engineering at University College London, and the UK representative on the European Federation of Biotechnology Working Party on Education.

Biotech and the new genes

Stephen Oliver

Biotechnology. By John E. Smith.

Edward Arnold: 1982. Pp.72.

£2.95, \$8.95.

Essays in Applied Microbiology.

Edited by J. R. Norris and M. H.

Richmond.

Wiley: 1982. Pp.540. £19.88, \$46.90.

Plasmids. By M. J. Day.

Edward Arnold: 1982. Pp.51.

£2.50, \$8.95.

Principles in Gene Manipulation, 2nd Edn.

By R. W. Old and S. B. Primrose.

Blackwell Scientific/University of

California Press: 1982. Pp.214.

£6.50, \$13.95.

BIOTECHNOLOGY requires the integration of a number of conventional disciplines: microbiology, genetics, molecular biology, biochemistry, chemistry and chemical engineering. It is the sort of subject which causes the universities, with their traditional departmental structures, considerable problems which may often only be solved by the introduction of post-graduate courses.

To write a text on biotechnology of just 75 pages designed for advanced high-school students and undergraduates would seem, therefore, to be an act of great temerity. Professor Smith has dared and won. His *Biotechnology* is a very readable and highly stimulating account which concentrates on the biological aspects of the subject. Fermenter design is discussed but product recovery is a lamentable omission. I was also surprised to find no reference to biotransformations. However, in the limited space afforded him the author has done an excellent job and his determinedly optimistic style should attract many students to the subject.

The editors of *Essays in Applied Microbiology* make no pretence of producing a comprehensive text and, inevitably, many will disagree with their choice of topics. This collection is intended for the same audience as Smith's book but most contributions are pitched at far too high a level.

As with its predecessor (*Essays in Micro-*

biology) individual chapters will be sold as separate units, an innovation welcomed by students and teachers alike. My "best buys" from this collection include "Single-cell protein production" by Norris, which, although written in the heady days of the commissioning of ICI's Pruteen plant, gives a measured evaluation of the biological, engineering, politico-economic and even moral constraints and incentives which impinge on the production of microbial protein; "Applied microbiology — a personal view", by Demain, a singularly uninformative title for what proved to be a masterly account of the physiological and genetical tricks which can persuade microbes to deregulate the synthesis of some desired product; and "Production of enzymes by fermentation" by Barfoed. Although this last chapter is marred by typographical errors (including mis-spelling of the author's name!), it provides an excellent account of production methods in the enzyme industry and emphasizes downstream processing.

The other Institute of Biology text — *Plasmids* by M.J. Day — was disappointing. It is rather superficial and lacks any treatment of eukaryotic plasmids or of recombinant DNA technology. There are also confusing errors such as the statement that ethidium bromide *increases* the density of DNA. The author's aim was to give an ecological and evolutionary perspective to his account. While many would agree that it is artificial to separate phage and plasmid genetics, it is difficult to cover both in 50 pages (lambda merits just one paragraph); it would have been more sensible to deal only with the plasmids.

In the world of books, a new edition is the sincerest form of flattery. The fact that the second edition of Old and Primrose's *Principles in Gene Manipulation* has appeared only a year after the first is testimony to both the speed of development of recombinant DNA technology and the industry of the authors. Their text has rapidly become a standard and deservedly so. Designed for those with "a reasonable working knowledge of molecular biology", it makes few concessions to the beginner. Advanced undergraduates and researchers at all levels will find the book invaluable.

The new edition is considerably extended and includes a new, but already dated, chapter on cloning in *Bacillus* and yeast. Useful appendices characterizing popular restriction enzymes and vector molecules have also been added, but the glossary is still inadequate. In their preface the authors express the hope that the field has reached steady-state and that they will not have to re-write their book too frequently. They, but not their readers, are doomed to disappointment. □

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Resolution & contrast

A.J. Lacey

Fundamentals of Light Microscopy.

By Michael Spencer.

Cambridge University Press: 1982.

Pp.93. Hbk £10, \$19.95;

pbk £4.50, \$7.95.

In *Fundamentals of Light Microscopy* Dr Spencer illustrates very successfully that the image a microscopist sees must be the subject of two interpretative estimates: first, of how far it is a true replica of the specimen under investigation; and second of what it portrays of the interaction between light and matter.

The ways in which the images are built up in the various forms of microscopy are explained in sufficient detail, including a sprinkling of mathematical support, to be an intellectual challenge. The book, however, is also useful in a practical sense. Although purporting to be about fundamentals, and although referring on no less than six occasions to the measurement of mass of small objects (sperm heads) — perhaps by implication a tribute to Howard Davies of King's College, from whose course the book springs — there is

otherwise only brief mention of measurement alongside the fuller treatment of magnification, illumination, resolution and contrast.

The Abbe approach to the understanding of image formation and the implied limit to resolving power of the microscope is nicely set alongside the part played by lens aberration correction to achieve detail and quality in the image. Contrast, however, a topic central to modern optical microscopy, is a little less well integrated. For example, the section dealing with the zero order of diffracted light should in my view have emphasized that there is a total reversal of contrast when it is prevented from contributing to image building. Also, I would have liked the author to have included rather more on incident light techniques, even for those readers primarily interested in transmitted systems.

Nonetheless this is one of the best of the small books of microscopy available. The coverage of interference reflection and total internal reflection microscopy gives it a modern appeal, most appropriate for the student of microscopy in the 1980s. □

A.J. Lacey, a Lecturer in the Department of Biology at Brunel University, is organizer of the Royal Microscopical Society's course "Principles of Light Microscopy".

Principles pictured

E.D. Saggerson

Principles of Biochemistry.

By Albert L. Lehninger

Worth: 1982. Pp.1,011. \$33.95, £15.

Human Biochemistry, 10th Edn.

By James M. Orten and Otto W. Neuhaus.

Mosby: 1982. Pp.1,120.

\$25.95, £23.25.

Biochemistry Illustrated.

By Peter N. Campbell and Anthony D. Smith.

Churchill Livingstone/Longman: 1982.

Pp.216. \$18.75, £8.25.

NINETEEN eighty-two was the year in which Lehninger was born again — not in some amazing religious experience, but in the appearance of *Principles of Biochemistry*. As he says, it is a new textbook and not a reworking of *Biochemistry* (Worth, 2nd Edn 1975). This is a good, readable book.

Both *Principles of Biochemistry* and Orten and Neuhaus's *Human Biochemistry* are substantial books intended to cover the main areas of biochemistry, though with a strong bias towards the mammalian side; as such, both are particularly suited to the needs of students in medical and other health sciences. Lehninger should also have appeal for science-orientated undergraduate courses. Neither book assumes a strong background in physical or organic chemistry on the part of

the student, and neither should be regarded as a detailed specialist source for graduate students.

The layout of *Principles* is reminiscent of Stryer's *Biochemistry* (W.H. Freeman, 2nd Edn 1981), though not as visually striking because of the use of only red and black rather than the excellent three-colour printing of Stryer. *Principles* is nonetheless replete with excellent illustrations, tables and photographs (almost 850). The text is broken into small compact sections by the use of headlines, and there is extensive use of underlining to emphasize new terms, names or important concepts. Lehninger has also adopted the use of boxes, though it is not always clear why some topics are selected for this honour.

In comparison *Human Biochemistry* is rather short on figures and illustrations, and overall is less attractive because the only colours used are black and a rather dull green. In some instances the apparent reluctance to resort to good diagrams is extraordinary, for example in explaining the regulation of haemoglobin function, immunoglobulin structure and function, biochemical separation techniques and X-ray diffraction. Both books make a serious attempt to relate to human aspects of biochemistry and the molecular basis of disease. The relevant chapter in Orten and Neuhaus, however, is rather a lengthy list and catalogue of disease states and therefore disappointing. Lehninger includes an excellent section entitled "Molecular Transmission of Genetic Information" which starts from first principles and

finishes with an exciting exposition of the techniques and the future possibilities of cloning experiments. The corresponding section in Orten and Neuhaus is rather less stimulating, and perhaps the fact that it is entitled "Genetic Control of Metabolism" is an important clue to the more metabolic and physiological emphasis of the book.

In both books each chapter is followed by an extensive and up-to-date list of reviews and monographs for further reading. These are better presented by Lehninger who categorizes the references rather than just presenting them as one long list. In addition, in Lehninger each

chapter is also followed by sets of problems which are very imaginative — and the answers are given at the back of the book.

At first I was rather uncertain about *Biochemistry Illustrated*. After further deliberation I feel that this is an interesting and potentially valuable new venture. The book is unconventional in being, in essence, 200 or so pages of clear diagrams and schemes, each illustration being supported by a concise explanatory text of 5–10 lines. The fundamentals of mammalian metabolism and molecular genetics are covered. The authors' special interest in medical education emerges in places.

It will be interesting to see what niche this book eventually comes to occupy. The authors consider that it may serve to make non-specialists such as school teachers aware of the principal trends in biochemistry and that it may be of use to students in developing countries whose English may be limited. I also suggest that it may offer a suitable way of advertising the subject to students one wishes to entice into courses in biochemistry. □

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Facing the music of immunology

John Humphrey

Immunology: The Science of Self-Nonself Discrimination.

By Jan Klein.

Wiley: 1982. Pp.687. £62.10, \$93.10.

JAN KLEIN is a highly respected immunogeneticist. Many might have thought of him as an immunologist, but not so himself. In his preface he states

I have a confession to make: when I started to work on the book, I knew little immunology. I knew something about one branch — the one I am actively involved in — but next to nothing about the rest Finally, I decided to do something about my appalling lack of knowledge; I decided to write a textbook of immunology. So, in contrast to most authors — who undoubtedly write textbooks for the very noble goal of educating their students, I wrote this book for the very egotistical reason of educating myself.

The result is the most complete textbook of immunology comprised within one cover that I know. It has been compiled partly from the author's own knowledge, but mainly from a highly intelligent culling from up-to-date reviews and books on different aspects, larded with bits of history and with references to works of art which have struck Jan Klein as apposite, and which lighten the generally erudite exposition.

One admirable consequence of his approach has been that where the experiments from which the data were derived are complicated, and the explanations require clear thinking and clear exposition (both by the author and the reader), Jan Klein takes us with him through the whole argument. This involves setting out the underlying biological or biochemical mechanisms, describing the principles of the experiments, and using clear and often original diagrams to support the interpretations which are reached. He does not take it for granted, for example, that the reader will carry in his or her head the alphabetic notation for amino acids used in peptide se-

quences, or the major histocompatibility determinants of different strains of mice and recombinants, but sets them out in tabular form. The book in fact contains many tables of relevant data (e.g. gene sequences, amino acid sequences, lists of macrophage products, lymphokines, HLA determinants, immunoglobulin allotypes, complement components) which would otherwise have to be sought in specialized books and articles.

The structure of the book is described as a symphony, with a first movement about history, a second about structure (of the animals, the organs, the receptors and the molecules involved), a third about mechanisms (macrophage, T-lymphocyte and B-lymphocyte dominated), the fourth being the synthesis (defence reactions in action). The movements are given greatly dif-

ferent weight, with the more recent exciting discoveries about the evolution and control of the immune response having priority. But practically all aspects of immunology come in, including — though relatively superficially — clinical conditions.

All of this is an astonishing feat, even though the 667 pages of text are printed in double columns. It is a book for advanced students and teachers, rather than beginners, and would need to be supplemented by a textbook about the clinical conditions which do not necessarily make immunological sense before it could be taken as a guide to practice. Nevertheless, even at its price, I regard it as a best buy. □

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Membranes-how they work, what they do

Michael Selwyn

Membrane Biochemistry.

By E. Sim.

Chapman & Hall/Methuen: 1982.

Pp.80. Pbk £2.95, \$6.50.

Dynamics of Biological Membranes:

Influence on Synthesis, Structure and Function.

By M.D. Houslay and K.K. Stanley.

Wiley: 1982. Pp.330. Hbk £23, \$52.65;

pbk £8.90, \$19.95.

Chloroplasts and Mitochondria, 2nd Edn.

By Michael Tribe and Peter Whittaker.

Edward Arnold: 1982. Pp.84.

£3.10, \$8.95.

Mitochondria, Chloroplasts and Bacterial Membranes.

By J.N. Prebble.

Longman: 1981. Pp.377.

£12.95, \$26.

SEVERAL sub-cellular organelles, including mitochondria and chloroplasts, are fundamentally specialized membranes, and their activities cannot be understood without a thorough grounding in membrane biochemistry. It is this principle that

links together the four books reviewed here, although they quite clearly split into two groups. Sim with Houslay and Stanley are concerned with the properties of membranes, while Prebble and Tribe and Whittaker write from the viewpoint of the activities of the organelles.

Sim's *Membrane Biochemistry* is an admirable little book which is very readable and informative about the lipid and protein components, structure, biosynthesis and assembly of biological membranes (membrane functions are the subject of another but unfortunately dated book in the same series). The material is of necessity presented in a concise form but full reference to reviews and to the original literature is provided. Very occasionally compression renders a passage potentially misleading but my major criticism is that some of the diagrams are very poor indeed (freeze-etching suffers in both respects). Overall the book is good reading for final-year undergraduates and also provides their teachers, or research workers, including non-specialists, with an excellent up-to-date survey.

In *Dynamics of Biological Membranes*, Houslay and Stanley emphasize the roles of fluidity and motion in membrane processes, and their evident enthusiasm for their subject aided by the excellent photographs make a stimulating book. The

same topics covered by Sim are dealt with, usually at greater length; in addition an account of membrane functions is included. It is disappointing, however, that the development of the dynamic picture of the membrane organization seldom leads to a full description of a membrane function. This is particularly noticeable in the chapter on transport processes, although there are good introductions to some of the more physiological functions. The omission of a full reference list is serious and there are also too many contradictions, repetition and other careless errors. Despite its faults *Dynamics of Biological Membranes* should be provocative reading for those, especially postgraduate students, doing research on membranes — but the lack of references is a real nuisance for teachers, and the errors and variability in treatment are a drawback for undergraduates.

Chloroplasts and Mitochondria by Tribe and Whittaker is intended to introduce sixth-form students to the structure and assembly of these organelles as well as to their roles in photosynthesis and respiration. The book starts with a confusing and laboured account of the role of ATP in bioenergetics which is followed by errors and poor judgement in the chapter on chemical reactions, including an inaccurate description of chemiosmotic coupling. Several of the photographs are far from clear, the separate chapter on history is of doubtful worth and the final chapter on practical work is too brief to give great hope of success. In all, the book is very far from ideal for its intended readers who are too inexperienced to cope with the deficiencies.

In *Mitochondria, Chloroplasts and Bacterial Membranes*, Prebble recognizes the similarities between the two organelles and bacteria and the value of a combined treatment. He gives comprehensive and accurate descriptions of the metabolic, bioenergetic, transport and biosynthetic processes of mitochondria and chloroplasts but has had to be highly selective in dealing with bacteria. Two relatively short chapters deal with bacterial energy transformation and bacterial photosynthesis. Two pages on bacterial transport processes seems excessively short and I thought it rather mean to include mitochondrial evolution in a bacterial chapter — a final chapter on the evolution of mitochondria and chloroplasts would have been a great improvement.

Overall this is a valuable compendium of information on chloroplasts and mitochondria combined with an introduction to bacterial bioenergetics. It should be useful to university teachers, students and research workers, but more so for those working on mitochondria or chloroplasts than for those whose interests lie with the bacteria. □

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Neuro this, that and the other

Maria Fitzgerald

Principles of Neuroanatomy.

By Jay B. Angevine, Jr. and Carl W. Cotman.

Oxford University Press: 1982.

Pp.393. Hbk \$32.50; pbk

\$17.95, £8.95.

Basic Neurochemistry, 3rd Edn.

Edited by George J. Siegel et al.

Little, Brown: 1982. Pp.826. \$30.75.

An Introduction to Neurophysiology.

By J.F. Stein.

Blackwell Scientific/Mosby: 1982.

Pp.385. £12, \$19.95.

Comparative Neurobiology.

By P.J. Mill.

Edward Arnold: 1982. Pp.280.

£9.95, \$19.95.

THESE days it is not sufficient for a neuroscientist to be solely a physiologist, an anatomist, a chemist or a behavioural scientist. Too often, the anatomist fails to realize that not all connections may be functional, the physiologist loses sight of the way an animal behaves and the neurochemist does not put his molecular hypotheses in the context of the functioning brain. For students of neuroscience, this is especially important. Aspects of neurobiology taught in different departments may appear to bear little relation to one another, and much of the excitement of the brain sciences is lost in a string of unrelated facts.

Textbook writers have recently become aware of the problem and we are now witnessing the advent of a new generation of neuroscience texts aimed at overcoming undue segregation of the subject. Neuroanatomy in particular is found by many students to be difficult to assimilate and relate to the living brain; yet without it we are lost, having no framework on which to build. For this reason Jay Angevine and Carl Cotman's *Principles of Neuroanatomy* is a wonderful book. Aimed to supplement a basic anatomy text such as A. Brodal's *Neurological Anatomy* (Oxford University Press, 1981) or M.B. Carpenter's *Core Text of Neuroanatomy* (Williams and Wilkins, 1978) rather than to be used alone, it is a joy to read.

Here is a book that makes neuroanatomy come alive, that brings together all the facts and gives them some meaning. It has a chatty, easy style but the contents are accurate and concise. The sections on

thalamus, reticular formation and limbic system are particularly good and there is an up-to-date section on chemical coding. Clinical and psychophysical data are well covered, and there are frequent references, by analogy, to everyday matters.

Another book which can be highly recommended to both student and research worker is the third edition of *Basic Neurochemistry*. Here the detailed and complex subject of biochemistry of nervous tissue is put in the context of other branches of neuroscience. Coverage ranges from basic neurocellular anatomy and physiology to clinical disorders and behavioural science. There are chapters on neurotransmitters, cell motility, brain energy metabolism and many more topics, all written clearly and concisely with up-to-date references and a good index. Amongst the neurosciences neurochemistry has made some of the greatest advances in the past few decades and that is reflected in the book.

In comparison to these last two books, Stein's *An Introduction to Neurophysiology* seems distinctly old-fashioned. This is particularly disappointing since the author aims to convey "the fascination and excitement" of neurophysiology, which is so lacking in many textbooks. This admirable aim, however, is never realized. The book has a fairly classical description of electrical properties of neurones, sensory and motor systems and goes on to reward, learning and memory. As such it has little to offer over other concise texts such as *Fundamentals of Neurophysiology* edited by R.F. Schmidt (Springer-Verlag, 1978), and in places is less accurate. There are good chapters, however, those on motor control being the best. The subject is approached from the end-point, a movement, which is then broken down into its constituent parts and the result is successful. But the book as a whole, although perfectly adequate and sound, is never stimulating. The excitement of neurophysiology comes from its attempt to give a functional perspective to anatomy and chemistry and provide a mechanism for behaviour; without this it becomes a series of important but rather dry observations.

Another new book intended as an introductory text is P.J. Mill's *Comparative Neurobiology*. As such it is inadequate, with very limited treatment of the central nervous system and few references. Where it does score is in its comparative approach. The author describes the anatomy, physiology and pharmacology of nerve and muscle by using constant examples from both vertebrates and invertebrates. This book is not sufficient for undergraduates coming to neuroscience for the first time, but it is full of fascinating facts with particularly good chapters on sensory receptors and on the control of behaviour in different species. It is a book for the true, all-round neuroscientist. □

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Companion to Kornberg

W.H. Freeman have issued a 1982 *Supplement* to Arthur Kornberg's textbook *DNA Replication*, which was first published in 1980 and reviewed in *Nature* 289, 718 (1981). The *Supplement* covers developments in the subject up to January 1982, and costs £7.50, \$10.

A line of classical physiology

P.D. Wall

The Senses.

Edited by H.B. Barlow and
J.D. Mollon.

Cambridge University Press: 1982.

Pp.490. Hbk £30, \$59.50;

pbk £12.50, \$19.95.

THE Senses has been written for undergraduate courses for medical students and others concerned with the topic. Some 60 per cent of it is reasonably devoted to the visual system, with a further 20 per cent on the auditory system. The remainder covers the vestibular system, the cutaneous senses, and smell and taste. Each chapter has a brief bibliography of suggestions for further reading, including general reviews and special references.

Many senior teachers of physiology will find this book satisfying, classical and

central. More junior research workers may find it puzzling, eccentric and parochial. For example, a paper is recommended with "read this if you have only a little time to prepare for a tutorial essay"; and an old book which missed the point even in its day is "by an intellectual for intellectuals". In addition there are some curious inconsistencies, such as the chapter on neuroanatomy of vision which makes no reference to the multiple visual pathways alluded to later in the book. The chapter on skin nudges into the 1970s with an attitude unchanged from the 1870s.

A reader of this year's proceedings of the American Neuroscience Society would have difficulty in many areas if he were to search *The Senses* for the background to the issues which today enthral the research worker. That, however, might be an unfair test for a book which intentionally succeeds in presenting clearly a particular line of classical physiology. □

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Two-faced toxicology

T.A. Connors

Principles and Methods of Toxicology.

Edited by A. Wallace Hayes.

Raven: 1982. Pp.750. \$84.32.

Principles of Biochemical

Toxicology.

By John A. Timbrell.

Taylor and Francis/J.K. Burgess Inc.:

1982. Pp.245. £13.50, \$28.50.

UNLIKE research into, say, oncogenes or recombinant DNA technology, toxicology is not popularly thought of as a glamorous subject. Nevertheless, it is arguable that toxicology is one of the most important areas of medical research since the causes of many serious human diseases are not known and most may eventually be proven to be due to "environmental" and hence preventable factors. A further problem for the student is that the subject may seem to be rather ill-defined: the scientist investigating the impact of pesticides on flora and fauna, the clinician studying the effects of drug abuse and the industrialist evaluating the safety of a novel chemical can all rightly call themselves toxicologists. So it comes as no surprise to find that the two volumes reviewed here are quite different, even though they both have the word "toxicology" in their titles.

As is made clear in the preface, the authors in *Principles and Methods of Toxicology* do not attempt to go in great detail into the mechanisms by which chemicals cause specific damage to biological tissues, but rather deal with the methods used to determine whether or not a chemical is likely to be hazardous to human beings. This corner of toxicology

nevertheless covers a very large area, but here it is coped with very successfully and lucidly. Successive chapters deal with acute and chronic (including carcinogenicity) testing and with more specialized techniques such as inhalation toxicity and skin and eye testing. Detailed accounts are given of the methods used to detect specific toxicity in all major organs of the body. Toxicity to the fetus is also considered as well as newer aspects of toxicology such as behavioural and immunotoxicology. The book concludes with a chapter on pharmacokinetics and, importantly, with a discussion of the knotty problem of extrapolation to man.

All in all I found this an excellent book and would endorse the editor's words in saying that the volume will be of particular value to students and others who have not yet entered a specialized field of toxicology. Indeed I would go further, and suggest that scientists involved in safety evaluation — especially those in government who are responsible for aspects of the regulation of chemicals — will also find it useful.

As suggested by the title, Timbrell's book is the other side of the coin and deals particularly with the biochemical basis of toxicology. However, again because of the complexity of the subject, no attempt is made to review all that is known about biochemical mechanisms. The book reflects the author's own interests and concentrates on the principles of

pharmacokinetics, drug disposition and metabolism, although there are also concise but interesting accounts of the types of toxic response to foreign chemicals and of mechanisms of selective toxicity to specific tissues.

I do have a small criticism of this book. Some important areas of toxicology, for example heavy metals, are dealt with so briefly as to imply either that they are unimportant or that little is known about them. To state, for example, that little is known about the relationship between inhibition of acetylcholinesterase and delayed neurotoxicity is to ignore the excellent work done in this field on mechanisms (although to be fair a reference to one of the many reviews in this area is included in the bibliography). I would also take issue with the assertion on p.127 that cancer induction is an irreversible change. Enough is already known about repair mechanisms, transforming growth factors and the reversibility of promoters to hold out some hope that when we know more about the complex process of cancer induction some cancers will prove to be reversible.

Nevertheless the major sections of the book are excellent, explaining biochemical mechanisms clearly and succinctly, with many first-class diagrams and figures. *Principles of Biochemical Toxicology* is certainly to be recommended, especially to its intended readership of undergraduate students. □

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There is no "why?"

Stuart Sutherland

Visual Information Processing.

By Kathryn T. Spoehr and Stephen
W. Lehmkuhle.

W.H. Freeman: 1982. Pp.298.

Hbk \$21.95, £17.80; pbk £10.40.

THE cant phrase "information processing theory", despite its savour of novelty and precision, means no more than the attempt to specify the mechanisms underlying the performance of some task; with the exception of the extreme behaviourists and a few cranks like J. J. Gibson, all experimental psychologists since about the beginning of the century have pursued this approach. It is neither novel nor is it characterized by precision. Information processing theorists do not aspire to the rigour of working computer programs, they are content with flow-charts which often contain boxes with labels such as "Recognition" and which are more a means of concealing our ignorance than dissipating it.

One would expect anyone bent on pursuing an information processing approach

Gardner in Britain

Next week Oxford University Press will publish a paperback edition of Martin Gardner's *Science: Good, Bad and Bogus*, the first time the book has been available in Britain. For review see *Nature* 295, 351 (1982). Price of the new edition is £4.95.

to vision to start by specifying the tasks carried out by the visual system and by identifying the relationships between the visual image and the real world that make the execution of each task possible. Spoehr and Lehmkuhle, however, like many other psychologists, are so carried away by their reckless quest for data that they forget about function. Whether they are discussing the black choroid coat of the retina or the use of features in recognition, they never ask the question "Why?". Instead they pour out a flood of recent "discoveries", many of which have an air of banality: the more eye movements someone makes when looking at a picture, the better he remembers it; pictures in which sections have been jumbled around are harder to process than normal pictures; an intervening verbal description provided by the experimenter can alter memory for a picture. One feels the results of such experiments would only have been worth reporting had they come out in the opposite direction. A few findings, such as the

discovery of the iconic store, and some of the recent work on imagery, are of more interest. Spoehr and Lehmkuhle describe them all with equal enthusiasm.

Visual Information Processing is, for the most part, clear and since there are few other texts reviewing the last dozen years' work in the area it will undoubtedly be used. It will, however, appeal only to students who like the cosy safety of learning experimental results by heart, and who do not want to be made to think. It contains a few howlers, for example, "Objects at a distance appear smaller" where the context makes it clear that the authors should have written "have smaller visual images" (p.34). It is a pity the authors have not devoted less space to the obvious and attempted to relate the results they report to the function of the visual system. □

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Knowing psychology

P.E. Bryant

History and Systems of Psychology.

By James F. Brennan.

Prentice-Hall: 1982. Pp.374.

\$25.45, £20.35.

Conceptual Issues in Psychology.

By E.R. Valentine.

George Allen & Unwin: 1982. Pp.200.

Hbk £12, \$25; pbk £5.95, \$9.95.

"WHO knows psychology who only psychology knows?" is a paraphrase which ought to be dinned into every new student of the subject. It is inconceivable that anyone could become a reasonable psychologist without also learning a great deal about its philosophical background and about neurophysiology too. Some knowledge of linguistics and of the workings of computers can also be a great help.

This is a lesson which students usually take some time to learn. One reason for their slowness is that psychology's connections with other subjects are rooted in its history, which on the whole has not been described entertainingly. The histories of psychology available to students are for one reason or another definitely daunting, which is a great pity because it means that many students end up learning nothing historical and therefore knowing little about the reasons and the assumptions behind much of the current research in psychology.

James Brennan's simple and attractive textbook is an attempt to stop this particular gap, and on the whole it does so very successfully. Its breadth is staggering, starting as it does with the Greeks, going on with some panache to the Renaissance, and then step by accurate step through to the

birth of psychology in the nineteenth century. The book culminates with a stimulating account of the early psychological schools and finishes with a brief summary of contemporary trends. The way in which the author manages to marshal such a large and varied cast and in the end to produce a coherent story is truly impressive. Of course in so few pages each strand receives rather short shrift, but there could not be a better, simpler start for a student who wants to know about the history of the subject and also to learn how to cope with those other, weightier and more forbidding historical tomes.

Elizabeth Valentine's book is as successful, but in a different way. She writes about the concepts and assumptions behind a lot of contemporary, empirical psychology. Many of the questions which she poses are as philosophical as they are psychological. Free will, the mind-body problem, what is meant by consciousness, the role of the theory — our inability even now to be sure about these familiar problems is a good enough illustration of our need for a sound philosophical framework.

Again this book is meant for students, and it is written simply and attractively. Each chapter presents the main points of view so directly that no room is left for confusion. Often Dr Valentine makes little attempt to resolve the arguments one way or the other, but that is not the main concern of her book. There could hardly be a better exposition of psychology's conceptual problems, and any student who reads both Dr Valentine's book and Dr Brennan's will understand the reasons for some of the subject's most persistent problems and for many of its most notable successes too. □

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Chemistry on the rocks

Peter S. Liss

The Geochemistry of Natural Waters.

By James I. Drever.

Prentice-Hall: 1982. Pp.376.

\$37.15, £29.70.

Inorganic Chemistry and the Earth.

By J.E. Fergusson.

Pergamon: 1982. Pp.400. Hbk £20, \$40;

pbk £9.95, \$19.95.

Inorganic Geochemistry.

By Paul Henderson.

Pergamon: 1982. Pp.372. Hbk £21, \$42;

pbk £9.25, \$18.50.

Q. "What is a geochemist?" A. "Someone who knows little geology and even less chemistry". Since these books are all about geochemistry, and in view of the well-known put-down quoted above, is there anything much to be learnt from them? In brief, the answer is rather a lot.

Before turning to the individual books, a few words should perhaps be spared to try to undermine the rather outdated idea underlying the response to the above question. Indeed, I suspect the attitude embodied in that answer applies to most cross-disciplinary subjects. It is as though by trying to link two or more bodies of knowledge, the practitioners of inter-disciplinary subjects have somehow broken faith with their former co-religionists in the true unidisciplinary congregations — this in spite of the fact that the cross-disciplinary subjects have often attracted and trained excellent mono-disciplinary specialists. More important, however, is that, at its best, the synthesis of knowledge from different areas has produced something greater than the sum of the parts. The lateral thinking involved has created a whole new subject with a way of looking at things of its own.

Of the three books reviewed here, that synthesis of viewpoints is best achieved by Drever in *The Geochemistry of Natural Waters*. As the title suggests, the book focuses on natural waters (fresh, saline, and mainly unpolluted) and on the processes that control their composition. The subject matter is not constrained by externally imposed divisions, for example inorganic and organic effects are treated as necessary, and not compartmentalized according to some preconceived plan inherited from pure chemistry. This gives the book an internal unity, which is helped by the treatment of basic chemical, geological, biological etc. concepts largely as they arise, rather than in some preamble or glossary, as is often the case elsewhere. The author has a remarkable ability to explain complex ideas clearly, and I'm sure his book will be a great success with both students and teachers. Although its scope isn't as wide, Drever's book bears compar-

ison with Krauskopf's *Introduction to Geochemistry*, published by McGraw-Hill in 1967, which has been a favourite for years. Both authors have a rare ability to engage the reader, whatever his level, with new insights and fresh ways of looking at old problems.

The content of Fergusson's *Inorganic Chemistry and the Earth* is well summarized by its subtitle — *Chemical Resources, their Extraction, Use and Environmental Impact*. The book is not primarily concerned with the Earth in its natural state, but more with its mineral and

energy resources and how they can be extracted and utilized. This occupies about half of the text; the rest is about the impact of such anthropogenic activities on the environment. The level of explanation is about average for a textbook of this type. The real bonus of the book is the mine of information it contains. Almost every page is crammed with interesting detail, the scope of which, especially in the environmental half of the book, has to stray out of the inorganic domain into the living world.

Inorganic Geochemistry by Henderson is a thorough, rather than an inspiring text.

The author concentrates on igneous and metamorphic rocks and, although there are short chapters on continental and oceanic waters, there is virtually nothing on sedimentary environments. It is in the same mould as the much used *Principles of Geochemistry* by Mason (Wiley, 1966) but, of course, substantially updated. Professional hard-rock geochemists, in particular, should find this book of considerable use. □

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Horse for a course in environmental science . . .

R.W. Raiswell

Environmental Chemical Analysis.

By Iain L. Marr and Malcolm S. Cresser. Blackie/Methuen: 1983. Pp.270. £21, \$39.95.

QUANTITATIVE analysis, that work-horse of any chemical science, could fairly be considered a victim of its own success. The analytical armoury now contains a formidable array of weapons, the range and rapidity of which attest to the developments in instrumentation and automation. At the same time, however, increasing ease of measurement has encouraged unthinking data acquisition — and nowhere is this more apparent than in the burgeoning field of environmental chemistry. Yet environmental studies also pose new and particularly difficult problems, near the limits of analytical measurement and specificity. Horse-sense asserts that analysis can only be the art of the possible, but a meaningful approach may often be constructed by relying less on a single technique and more on a judicious combination of techniques, utilizing what I.A. Selby has termed the "synergism of analytical techniques".

The appearance of a new text, dealing with the problems encountered in environmental chemical analysis, is generally to be welcomed as encouraging a more holistic approach. Marr and Cresser's offering succeeds on several counts. First, it provides a basic framework for considering

analytical problems in the environment, giving due attention to the often-neglected aspects of sampling, sample preparation and sources of error. The text occasionally verges on the obvious, but does succeed in clarifying the requirements of an effective analytical strategy.

Secondly, the authors provide brief reviews of a number of modern analytical techniques, from both theoretical and operational viewpoints. Here the book is rather less successful in organization and coverage. The presentation of different techniques within the four environmental "spheres" is inevitably rather arbitrary and gives a restricted impression of broad spectrum techniques such as atomic absorption spectroscopy. Furthermore, whilst the breadth of coverage is to be applauded, it does lead to some curious omissions and imbalances. Instrumental

methods are emphasized at the expense of more traditional methods, for example titrimetric methods being discussed but twice and on neither occasion is reference made to the widely-used determinations of dissolved carbonate and hardness in water samples.

Nonetheless these are but minor criticisms. The overall treatment is consistent with the authors' objectives, and the text is well-written and suitably illustrated, with few errors. The tyro environmental chemist will find the details of analytical methodology a valuable feature, whilst the tutor will be attracted by the numerous environmental examples. □

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. . . out of the field

Roy M. Harrison

Environmental Science Methods.

Edited by Robin Haynes. Chapman & Hall: 1982. Pp.400. Hbk £20, \$39.95; pbk £9.95, \$19.95.

IN EACH of the traditional scientific disciplines there is an accepted basic body of knowledge which is taught to undergraduates over perhaps the first two years of their course, the students subsequently being allowed to specialize. There is rather little variation in that basic material between university courses throughout the world.

Environmental sciences, however, is far from being a traditional discipline and there are almost as many approaches to teaching and content as there are available courses. One of the broadest courses in the United Kingdom is that offered by the School of Environmental Sciences at the University of East Anglia, from which this book emanates. In the words of the editor, "it is intended to provide a selection of methods for students taking university courses in geography, geology, meteorology, hydrology, soil science, ecology and other allied environmental sciences".

Two facets of the book struck me forcibly. An immensely important aspect of experimental work in the environmental sciences is fieldwork; it occupies a substantial percentage of the overall practical part of the course we run at Lancaster. Apart from a chapter on surveying, this book ignores fieldwork almost totally. Useful topics might for example have included meteorological observation techniques, river discharge gauging, geophysical prospecting methods, and water and air sampling for pollutant determination. The other striking aspect is the variability in level of treatment: the mathematics and statistics are covered in depth and are likely to be of considerable value to the student, whilst some other topics such as computing and chemical laboratory methods are given such insubstantial treatment as to be of little use.

Despite its considerable length, *Environmental Science Methods* is as notable for its omissions as its coverage. A text of more limited scope might have offered the editor a more worthwhile task. The book will, however, prove a useful practical guide to students in some of the areas covered. □

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Textbook supplement — prices

Where appropriate, both dollar prices pertaining in the United States and sterling prices for the United Kingdom are given in the bibliographical details for each book. Export prices will generally be higher. If a dollar or sterling price is not cited, the book is not available in one of the two countries. However readers should check both price and availability of books before ordering.

An index to all of the books reviewed in this issue appears on pp.192-193.

Changing the shape of geomorphology

C. Kidson

The Nature of Geomorphology.

By Alistair F. Pitty.

Methuen: 1982. Pp.160. Pbk £3.95, \$6.95.

Process and Landform.

By Alan Clowes and Peter Comfort.

Oliver & Boyd/Longman: 1982. Pp.290. £4.95, \$9.95.

Geomorphological Field Manual.

By V. Gardiner and R. Dackombe.

George Allen & Unwin: 1982. Pp.272. Hbk £16, \$30; pbk £7.95, \$15.

THE RATE of change of science is now so fast that a periodic re-statement of aims and objectives in each of its component disciplines is essential. Geomorphology is no exception to the general necessity. In this context it is most appropriate that Alistair Pitty has attempted to review the current status of the field.

No one would, in 1983, view geomorphology in the light of, for example, Wooldridge and Morgan's *The Physical Basis of Geography: An Outline of Geomorphology* (Longmans Green, 1937). In many respects, however, the earlier volume was a successful presentation of the state of the art at that time. *The Nature of Geomorphology*, by contrast, falls far short of reflecting the whole spectrum of geomorphological studies in the 1980s. In place of the careful and systematic reviews to be found in *The Physical Basis of Geography*, the reader is given a rambling, and sometimes confused, philosophical apologia which spends far too much time on pondering whether this part of the subject falls within the field of geology or of geography, and on whether or how geography relates to the social sciences.

While noting the swing to process studies and quantitative methods in the 1950s and 1960s and away from the earlier over-emphasis on "stage" or time in Davisian geomorphology, Pitty fails to give due weight to the swing back of the pendulum represented by the large number of geomorphologists who are now much concerned with Quaternary chronology. The closest he comes to recognizing this aspect of the subject is the almost regretful statement that "contemporary geomorphology's strengths are ringed around its multi-disciplinary periphery rather than congregated at its formal core".

In *Process and Landform* Clowes and Comfort attempt a similar task to Pitty but at a rather lower level, that of the sixth-former and the College of Education student. The format of the book has the merit of Wooldridge and Morgan's approach of systematically treating each area of the subject in turn. In many ways it is an exercise in presenting to schools a digest of research at

university level, and insofar as it succeeds in this it may be of value to first-year university students. Unfortunately in places it is less than successful and shows some of the worst aspects of basing school lessons on half-digested undergraduate lecture notes. The diagram on "Britain During the Pleistocene Glaciations" (on p.202) exemplifies this failing. It is, in other words, a useful text but not without serious blemishes.

The systematic presentation of material in Gardiner and Dackombe's *Geomorphological Field Manual* is also in sharp contrast to the style of *The Nature of Geomorphology*. The authors' aim is to provide an *aide mémoire* rather than a manual of field techniques. In this they succeed admirably, although not every field

geomorphologist would agree with their choice of material. As in the Pitty volume the emphasis is heavily on process studies, the only concession to the role of time being a very short paragraph on the collection and storage of samples for ¹⁴C dating. Nevertheless the *Manual* represents a useful contribution to field work in that part of the subject to which it relates.

Any layman attempting to understand contemporary geomorphology by reading these three texts would find some enlightenment. Many geomorphologists performing the same exercise might be dissatisfied with some aspect of each. □

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The geologist at the restaurant

Keith Bell

Putnam's Geology, 4th Edn.

By Edwin E. Larson and P.W. Birkeland.
Oxford University Press: 1982. Pp.780. £12.50, \$25.95.

Earth, 3rd Edn.

By Frank Press and Raymond Siever.
W.H. Freeman: 1982. Pp.610. Hbk \$25.95, £20.50; pbk £11.95.

Physical Geology, 6th Edn.

By L. Don Leet, Sheldon Judson and Marvin E. Kauffman.
Prentice-Hall: 1982. Pp.483. \$30.75, £24.60.

IT IS somewhat surprising, considering the scope of the earth sciences, that writers of modern, introductory textbooks broadly agree on what should be taught, what should be emphasized and the depth to which such material should be covered. Although the ingredients are roughly the same, the selection of a text, like a favourite restaurant, depends on how the ingredients are handled, how they are prepared and how they are served. When three past winners enter a race it becomes subjective, a matter of taste, as to which menu should be chosen.

Putnam's Geology, first published in 1964, is a readable book, written with dedication in a distinctive, appealing style that most students will find attractive. Two new chapters, one on the Solar System and one on energy and resources have been added to this new edition. Although profusely illustrated, the quality of the illustrations tends to vary and the removal of the colour plates from the main body of the text to the centre of the book is not an improvement. Overall, the book is thorough, fairly broad in scope and enjoyable.

The new edition of *Earth*, neatly divided into three broad areas covering the

evolution of the Earth, surface processes and internal processes, includes such current topics as COCORP and overthrust belts, oceanic hot springs and pre-Mesozoic drift that bring a feeling of currency, so often lacking in introductory texts. The line drawings are particularly good and a new, large-page format is used. Novel features include the skilful use of footnotes (so hated by editors) and self-contained boxes, also found in the previous edition, that include such delicacies as "anchoring the isotherm" and "high pressure and shock experiments". The latter should appeal to the more curious student, without hampering the more general reader and detracting from the main body of the text. The quantitative handling of some of the data will also find favour among the science-stream students.

Lying somewhere between the two is *Physical Geology*, a streamlined volume, ideal for someone wanting a no-frills, head-on look at the earth sciences. Changes in the new edition include extensive revision of metamorphism and metamorphic rocks, and separate chapters on weathering and oceans. Relegation of sections about planetary bodies and space exploration to an appendix is somewhat puzzling, but at least such information is available. A sufficiently detailed table of contents allows most topics to be found quickly and easily.

Interesting features, common to all three books, are chapter summaries, geological glossaries (a boon to the non-scientist) and fairly extensive chapters on mineral resources and energy. Which to choose is difficult. *Putnam's Geology* is best described as plain, wholesome fare, Press and Siever's *Earth* as *la nouvelle cuisine* and *Physical Geology* falls in the "let's eat right to keep fit" category. Choosing any one of the three offerings would be gratifying — all have the potential for satisfying a hearty appetite. □

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Under the ocean

Peter J. Smith

The Sea Floor: An Introduction to Marine Geology.

By E. Seibold and W.H. Berger.
Springer-Verlag: 1982. Pp.288.
DM46, \$20.

SEIBOLD and Berger are in an unenviable position. They have come out with a 288-page introduction to marine geology within a year of the publication of an 813-page book with precisely the same aim and written by one of the world's best-known oceanographers. Moreover, the earlier book, James Kennett's *Marine Geology* (Prentice-Hall, 1982), though not flawless, has been universally praised, not least by myself (*Nature* 295, 466; 1982). Then it has to be said that *The Sea Floor* has been "developed" (the authors' word) from a previous book in German by Seibold, which means that the present version was not planned from the start as a coherent whole and is in large part a translation.

The book opens with chapters on the origin and morphology of ocean basins and margins, and continues with discussions of the sources and composition of marine sediments, the effects of waves and currents, sea level changes, and organisms on the sea floor. It then moves on to the effect of climatic zoning on marine

sedimentation and to palaeoceanography, ending, apart from a number of appendices, with a chapter on ocean floor resources.

The approach is straightforward, if somewhat uninspiring, and the content is not always as up-to-date as it might be. Among the intended audience are those "without formal training in the natural sciences"; but it is hard to take that very seriously, partly because there is little attempt at the beginning to set up marine geology as a topic worthy of the non-scientist's attention and partly because absolutely no effort has been made to present the book as anything other than a dull academic text.

Apart from price, the volume's one advantage over its rival is that it is a short, no-frills summary of marine geology and thus potentially useful to someone — an undergraduate, say — wanting a quickly-read overview of the subject before getting down to serious study. Even in this it is not ideal, however, because of its omissions, one of the most conspicuous of which is treatment of igneous petrology and geochemistry.

The Sea Floor must have seemed a good idea when it was proposed; the marine geology field was then almost free of introductory texts. It is the authors' misfortune to have been thoroughly trounced by Kennett. □

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Pictures of petrology

Bernard Elgey Leake

Elsevier's Mineral and Rock Table.

Compiled by P. Lof.
Elsevier Scientific: 1982. Dfl.40. Ten
copies Dfl.185, \$78.75.

THIS large (70 × 133 cm) wall-chart displays a wealth of information concerning the microscopic properties of igneous, metamorphic, sedimentary and ore-containing rocks.

The top two-thirds of the chart deals with the optical properties of minerals, arranged in six columns of rock-forming minerals (totalling 74 minerals) plus four columns of ore minerals (totalling 50). The former are classified by birefringence, colour and relief and are accompanied by a superbly-printed pair of colour photographs of each mineral in plane-polarized light and under crossed-nicols. Similarly with the ore minerals, which are classified according to anisotropy, isotropy, distinctive internal reflections and reflectance properties; again a pair of colour photographs shows each mineral under plane polarized light and crossed-nicols.

The photographs, totalling about 225, are the highlight of the chart. Their quality

is excellent and the choice of representative views is astute. Even muscovite and talc, which are effectively indistinguishable in thin section, are placed next to each other so that their similarity is apparent. Unfortunately, though, the obsolete terms oxyhornblende and barkevikite are retained.

The lower third of the poster diagrammatically shows the principal rock, meteorite and ore classifications, and includes a coloured birefringence chart.

The poster is intended for laboratories where students are working with microscopes and endeavouring to master mineralogy and petrology, but it will certainly also be helpful for graduate students and invaluable in tutorials. For all such users it can be strongly recommended. □

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Spring books

The next review supplement to appear in *Nature* will be Spring books, on April 28th. Among the books to be reviewed are Nicholas Wade and William Broad's *Betrayers of the Truth: Fraud and Deceit in the Halls of Science*, Dorothy Nelkin's *The Creation Controversy, Science and Moral Priority* by Roger Sperry, and Stephen Jay Gould's latest collection of essays, *Hen's Teeth and Horse's Toes*.

Pet rock-pourri

Bruce Sellwood

Sedimentary Structures.

By J.D. Collinson and D.B. Thompson.
George Allen & Unwin: 1982. Pp.240.
Hbk £18, \$40; pbk £8.95, \$17.95.

Sedimentary Petrology.

By Harvey Blatt.
W.H. Freeman: 1982. Pp.564.
Hbk £22.50, £22.20; pbk \$14.

Petrology: Igneous, Sedimentary and Metamorphic.

By Ernest G. Ehlers and Harvey Blatt.
W.H. Freeman: 1982. Pp.731.
\$29.95, £22.20.

Igneous and Metamorphic Petrology.

By Myron G. Best.
W.H. Freeman: 1982. Pp.630.
\$29.95, £22.20.

Igneous Petrology.

By C.J. Hughes.
Elsevier Scientific: 1982. Pp.550. Dfl.70, \$30.

THE complex mineral aggregates dismissed by the world at large as merely "rocks" are generally subdivided into sedimentary, metamorphic and igneous depending upon their origin. Sedimentary rocks are usually bedded and sometimes exhibit a variety of internal structures, and biogenic features, produced in response to processes acting at the time of deposition. The successful interpretation of sedimentary sequences depends on the acquisition of field data and its integration with later laboratory studies. There are, however, few elementary texts providing guidance on how field observations may be made or, indeed, on what pertinent questions should be asked in the face of an unknown outcrop.

Sedimentary Structures is essentially a teaching book designed, with the British undergraduate in mind, to fill this gap. It does so most successfully. As well as taking for granted that the reader possesses a basic knowledge of mineralogy and other sciences, the assumption is also made that he or she will regularly get wet and dirty, as all sedimentologists do.

It is a well organized book, commencing with a discussion on the nature of the bedding itself. (A rock sequence may represent some millions of years of time and yet contain individual beds that took merely hours or tens of thousands of years to accumulate.) Successive chapters deal with the properties of fluids and sediments, erosional structures, mudrocks, sandstones, gravels, chemical and biological structures and deformational structures. The final chapter indicates how observations can be assembled into depositional interpretations of sedimentary sequences and facies. Most topics are successfully considered with the exception of mudrocks. This book is excellent value, however, and can be recommended for students without serious reservation.

The remaining books deal with petro-

logy, the study of the occurrence, field relations, mineralogy, textures and relative abundance of rocks. *Sedimentary Petrology* is said to be aimed at the third- and fourth-year student in the United States and is a companion volume to *Petrology: Igneous, Sedimentary and Metamorphic*; indeed it is so companionable that large blocks of text are reproduced verbatim in the two books.

Sedimentary Petrology provides a more in-depth view of sediments and is thus more successful as a student text as it is clearly aimed in one direction. *Petrology*, on the other hand, attempts to cover the entire petrological field and fails to provide the critical, detailed source so essential to students graduating from honours courses, at least in Britain. Both books are attractively produced and mostly contain clear diagrams, but reference citation within the text is thin (the more so in *Petrology*), each chapter ending in a list of "further reading". Figures are, however, attributed to fully referenced sources. These books are clearly designed for, and most pertinent to, the American market and should do well there. I could not recommend either to a British student; better and cheaper texts exist.

Igneous and Metamorphic Petrology informatively covers all aspects of igneous and metamorphic petrology, ranging over global geochemistry, plate tectonics, isotope studies and basic thermodynamics. It is readable and well illustrated with line diagrams and monochrome figures. Fundamental principles are clearly and concisely introduced and it thus provides a good undergraduate text. However, the main weakness is that, like *Petrology*, it is insufficiently critical and does not investigate the models presented in any detail. This failing is anticipated by the author in his preface; consequently the book will only provide background reading for advanced undergraduates or postgraduates. It will not serve as a sourcebook for laboratory work either — the descriptive text and illustrations are inadequate — but as a general background text it could be most useful.

Igneous Petrology, too, is a readable book, with a reasonable coverage of some areas of the subject. Certain topics are, however, badly imbalanced — e.g. the section on phase equilibria is almost entirely devoted to a discussion of low pressure crystallization. There are some useful and interesting case studies of igneous provinces but in many cases the petrogenetic connections are thin or partial.

There are further drawbacks which lessen the value of the book. First, the rock classification used is idiosyncratic. It is said to be based on IUGS Commission proposals but these are not described and the connections are left unclear. The definitions provided are, in any case, too abbreviated and a student would still need a proper descriptive petrography. Secondly,

a few oddities exist (e.g. "petrology's residual system" p.194). But the greatest flaw is the absence of a number of landmark references — for instance to two of H.S. Yoder's seminal papers — leaving the student reader faced with crucial gaps in background material.

It is stated in the preface that the aim of the book is to bridge a gap. The gap is in any case a small one and this book falls into the chasm rather than bridging it. □

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In six dimensions

R.A. Howie

Crystallography.

By R. Steadman.

Van Nostrand Reinhold: 1982. Pp.120. £4.25.

Geometrical and Structural

Crystallography.

By Joseph V. Smith.

Wiley: 1982. Pp.420. £23, \$34.45.

An Introduction to Crystal Optics.

By P. Gay.

Longman: 1982. Pp.262. £6.95, \$14.95.

Nature of Earth Materials, 2nd Edn.

By Anthony C. Tennen.

Prentice-Hall: 1983. Pp.414.

\$23.30, £18.65.

Petrography: An Introduction to the Study of Rocks in Thin Section, 2nd Edn.

By Howell Williams, Francis J. Turner and Charles M. Gilbert.

W.H. Freeman: 1982. Pp.616. \$29.95, £20.95.

Atlas of Igneous Rocks and their Textures.

By W.S. MacKenzie, C.H. Donaldson and C. Guilford.

Longman/Halsted: 1982. Pp.147. £9.95, \$27.95.

THE subject of crystallography often makes its appearance as a brief, early chapter in many textbooks on materials science, physics, chemistry, geology and so on, but may leave the undergraduate with little more than an aversion to Miller indices. One answer for such students is to read *Crystallography*. The author presents the basic ideas simply, following them in the text with a succession of short questions. This is largely a book of illustrations and problems, with no lengthy expositions; the diagrams are particularly interesting. Although there are seven sections, it is not necessary to study the text systematically from the beginning: thus a student taking an X-ray photograph may begin with Section 5 and leave the rest until later. There are no stereographic projections.

Geometrical and Structural Crystallography is an altogether more advanced text, suitable for research workers or graduate students. Nevertheless it uses the simplest possible mathematics consistent with proper use of the concepts of symmetry theory, packing and topology. Each chapter becomes progressively more difficult and the book is designed so that the advanced topics can be omitted without upsetting the logical continuity. The

author rightly points out that crystallography is a hierarchical subject which collapses if logical or numerical errors are made and that it is essential to master each aspect before proceeding.

The text is very taut and closely argued; to dip in is to get ensnared. There are numerous cross-references and copious diagrams, and each chapter includes a series of graded exercises followed by answers (where appropriate).

Packing and crystal morphology are first considered in two dimensions, but then we are introduced to the study of polyhedra and onward, via stereographic projection, to the concepts of packing in three dimensions. The teaching of crystallography plays an essential role in the education of geologists, for example, not purely for the part it plays in mineralogy but mainly for the training it provides in thinking in three dimensions. Here the author's treatment of the ideal void-filling of close-packed structures as exemplified by spinel is instructive. The more rigorous approach via lattices and point groups in three dimensions follows, leading to band, rod, layer and three-dimensional space groups and to the concepts of anti- and colour-symmetry. The two final chapters deal with atomic packing and symmetry in crystal structures. This is a self-study text, produced by an experienced and inspiring teacher; attempting the exercises and drawing or constructing the appropriate models is an essential part of the book.

The paperback re-issue of the 1967 edition of *An Introduction to Crystal Optics* is to be welcomed, although only the bibliography has been updated since the first edition. The book blends clear theoretical explanations with a thorough discussion of practical microscope techniques and remains a comprehensive and authoritative textbook for students. It is particularly valuable on the interpretation and use of interference figures and on the dispersion of the indicatrix.

The second edition of *Nature of Earth Materials* is intended for use in a college course on rocks and minerals for non-science majors and is not aimed at advanced students of mineralogy and petrology. The text is readable and informative, but many of the black-and-white photographs are so poorly reproduced as to be worthless.

Petrography will be applauded by students of petrology at an intermediate level. Again this is a second edition, but the book has been extensively revised to take account of the spectacular advances in all branches of petrology in the past 30 years.

An acquaintance with rocks in hand specimen and with optical mineralogy is assumed. The two unifying themes throughout are the necessity to treat purely descriptive work in a manner consistent with modern petrogenetic concepts (requiring some knowledge of chemistry and of phase equilibria) and the field occurrence and global distribution of the various common rock types, with special emphasis on variations with tectonics and time; the text is illustrated with numerous, clear thin-section drawings. Comparison may be made with Hatch, Wells and Wells' *Petrology of the Igneous Rocks* (George Allen and Unwin, 1972), and Mason's *Petrology of the Metamorphic Rocks* (George Allen and Unwin, 1978), both of which have a somewhat similar style. The excellent drawings in the former have become familiar to generations of students through its 13 editions and are more informative than those of *Petrography*.

Atlas of Igneous Rocks and their Textures is a full-colour sequel to *Atlas of Rock-Forming Minerals in Thin Section* (Longman, 1981), one half being devoted to microphotographs of many of the common textures found in igneous rocks, and the second half illustrating the appearance of some 60 of the commonest igneous rock types. Nearly 300 colour photographs are included, with in many cases the same view shown in plane-polarized light and under crossed polars. Some of the nomenclature may be unfamiliar (I have been giving lectures on petrography for too many years without appreciating that, for example, in poikilitic texture the enclosed crystals are termed chadacrysts), but the specimens and textures are well chosen and the photography and colour reproduction are, in general, excellent.

Interestingly both works dealing with the petrography of igneous rocks fight shy of embracing the Streckeisen or IUGS classification with its foid-type nomenclature. Thus Williams and his colleagues use the time-honoured classification of Rosenbusch, with cross-references or footnotes where terminology differs significantly from the IUGS scheme, while MacKenzie *et al.* define each rock illustrated but claim that the names used are as near to consensus opinion as they can sense it. Thankfully both texts avoid the current fashion of using the ugly term granitoid which is so loose as to be meaningless.

With the earlier *Atlas*, complaints have been heard that some students attempt to identify minerals in thin section simply from the colour photographs without going through a proper diagnostic routine. Such short-cuts should not be a danger here as igneous rocks are so infinitely variable in texture and modal composition. This book will be universally acclaimed by students and teachers alike. □

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Academic questions of geological structure

D.L. Dineley

Basic Geological Mapping. By John W. Barnes.

Open University Press/Halsted: 1982. Pp.110. £4.95, \$12.95.

The Field Description of Sedimentary Rocks.

By Maurice E. Tucker.

Open University Press/Halsted: 1982. Pp.112. £4.95, \$12.95.

Introduction to Small-scale Geological Structures.

By Gilbert Wilson.

George Allen & Unwin: 1982. Pp.128. Hbk £10, \$20; pbk £4.95, \$9.95.

Introduction to Geological Maps and Structures.

By John L. Roberts.

Pergamon: 1982. Pp.332. Hbk £20, \$40; pbk \$15.

Foundations of Structural Geology. By R.G. Park.

Blackie/Chapman & Hall: 1982. Pp.134. Hbk £16.95, \$35; pbk £7.95, \$17.95.

A FEW YEARS ago publishers' representatives were anxiously enquiring where some of the more glaring gaps lay in the range of geological textbook coverage. The lack of small-to-medium-sized texts on field and structural geology was undoubtedly brought to their attention and the very positive response made over the past twelve months is to everyone's advantage.

In collaboration with Halsted Press and the Open University Press, The Geological Society of London has embarked upon publishing a series of handbooks for students. *Basic Geological Mapping* and *The Field Description of Sedimentary Rocks* are the first two to appear and they should be accorded a warm welcome. They are pocket-sized little volumes for the student to carry in the field for reference and use as he or she learns some of the most basic observational techniques that any geologist can acquire. There is no doubt that students find their early field training influences their subsequent progress to a marked degree. An enthusiasm for geology aroused at this stage seems to persist and to lead to a better understanding of the broader concepts in the subject than at any other. The style of writing in each book is simple and direct: the illustrations are numerous, clear and instructive. Line diagrams invariably help the text along and most of the (half-tone) photographs are good. The two further handbooks to come will be awaited with high expectations. This publishing venture by the Geological Society will, one hopes, be highly and deservedly successful.

Gilbert Wilson's *Introduction to Small-scale Geological Structures* makes a good complementary text to those just mentioned. In 1946 Wilson's paper on the relationship of slaty cleavage and kindred structures to tectonics came as a boon and blessing to students, such as myself, who had to struggle with such phenomena. Elegantly written and splendidly informative, it brought light to some fairly dim corners of the undergraduate syllabus. Now at last there is a treatment of small-scale structures in the same concise way and with similarly frequent reference to neatly described field examples. Illustrations here

also are appropriate and good. This is another valuable pocketful.

John Roberts's *Introduction to Geological Maps and Structures* takes its reader metaphorically over much of the same ground. It deals first with sedimentary rocks and the outcrop pattern, progresses to folds and folding, folded rocks and outcrop patterns, joints, veins and faults, and then to "igneous rocks and their structure" (sic). Unconformities and the geological record are accorded a chapter, and a concluding account of cratons and orogenic belts brings the reader to a consideration of the larger kinds of geological structures and terrains.

A chapter of perhaps wider interest since it directly concerns depositional events as well as those involving crustal movement is the one devoted to unconformities and the geological record. This describes the common range of unconformities and kindred phenomena and includes useful entries on synoptic cross-sections and palinspastic reconstructions. From these it is a short step to considering the nature of Earth movements and that "all-embracing branch of geology known as tectonics". Finally the climactic chapter, "Cratons and Orogenic Belts", is the grand view of how structural features in the crust are distributed and how they may originate. All of this is very good, readable and reasonable. It is well illustrated and lacks only one feature in its make-up — as does the entire book — not one word about the history of the development of structural geology and tectonics. This is noted by way of interest and is not a criticism of the book, which is undoubtedly very good value for money, nicely produced and highly recommendable on all scores.

A thought prompted by the last few pages and the appendix (list of Geological Survey Maps) is that there is reference to about 50 published British Geological Survey maps and half as many produced by the USGS but the book has seemingly not been concerned with geological cartography so much as geometry. No illustrations from the published geological maps mentioned are included. Isopachyte, facies and sediment ratio maps are given very scant treatment; attention is firmly

upon structural analysis. Tectonic maps are briefly discussed but not illustrated. This seems a pity, but no doubt the constraint of price forbids the inclusion of such luxuries.

The last of this set of five, R.G. Park's *Foundations of Structural Geology*, has much more to say about larger structures and about tectonics. It is direct and simple in its approach. There are three parts: morphology — how to describe and classify structures; deformation — how structures are formed; and geotectonics — major Earth structure. Not a word is wasted, not a diagram is superfluous and the diagrams are indeed excellent. There are a few well-chosen suggestions for further reading at the end of each chapter. All in all this, too, is a book to welcome for its clarity and coverage of the subject.

Each of the books reviewed here has been written by a university geologist, a man known for the research he has published and for his interest in propagating his discipline and chosen gospel. The academic profession is well served by such authors — not to mention the students. These five books are a good crop, one that will feed the appetites of many students for many seasons to come. □

D.L. Dineley is Channing Wills Professor of Geology and Head of the Department of Geology at the University of Bristol.

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High and wide

J.E. Guest

Introduction to Planetary Geology.

By Billy P. Glass.

Cambridge University Press: 1982.

Pp.470. £18, \$29.95.

IN RECENT years a number of books have been written on planetary geology at different levels for different audiences. Billy Glass's introduction to the subject is probably the most up to date and certainly covers a wider range of topics than other books of comparable intellectual level.

The presentation of topics is conventional, dealing with individual planetary bodies and groups of objects in the Solar System. After an introductory discussion of basic principles, there is a substantial chapter reviewing our knowledge of the Earth as a planet — this is particularly useful as students of planetary science come from a variety of disciplines and may not necessarily have a formal training in geology. There follows a section on meteorites and terrestrial dust, giving a comprehensive review of the state of the art in this field.

The fifth chapter, the only one which is specifically process-orientated, considers the physics of impact cratering and shock metamorphism; it is justifiable to consider impact separately for although it is a geological process it is rarely discussed in geological texts. The author then proceeds to cover tektites, the Moon, Mars,

Mercury, asteroids and comets, and the outer planets and their satellites, concluding with chapters on comparative planetology and a discussion of the origin of the Solar System. Frequently this last topic is dealt with at the beginning of books on planetary geology and thus the authors are unable to take into account the new data derived from planetary exploration that appears later in the book.

It is imperative that any book on this subject is well illustrated, making full use of examples from the tens of thousands of pictures now available. That requirement is certainly met here, with large numbers of high-quality pictures (and line-drawings) in the text as well as a special section of colour photographs at the beginning of the book. The author has managed to keep the text easy to read (although, inevitably, many topics are dealt with superficially) and the scientific literature is adequately referenced throughout the book.

During the past few years the number of university departments offering courses on planetary geology or more generally on planetary science has increased considerably. Only recently have suitable textbooks started to become available. *Introduction to Planetary Geology* will be more appropriate for those courses which attempt to cover a wide range of topics, but it could well be used with more specialist courses if supplemented by reviews and reports in the literature. □

John Guest is a Lecturer in Planetary Studies in the Department of Physics and Astronomy at University College London.

The gentle touch

David W. Hughes

The Physical Universe: An Introduction to Astronomy.

By Frank H. Shu.

University Science Books/Oxford

University Press: 1982. Pp.569.

\$28, £14.95.

Astronomy: From the Earth to the Universe, 2nd Edn.

By Jay M. Pasachoff.

Saunders: 1983. Pp.500. \$43.45, £25.50.

Astronomy: The Evolving Universe, 3rd Edn.

By Michael Zeilik.

Harper & Row: 1982. Pp.613.

\$41.60, £27.

THE MAIN difference between the astronomy textbooks of today and those of 60 years ago lies not only in the profusion of photographs and colour plates but also in the great care which authors and "art and design directors" nowadays put into the line drawings. Some think astronomy courses have blossomed because of the flood of "gee-whiz" discoveries. But it has always been so. What has changed is the

ease with which this new knowledge can be assimilated, thanks mainly to the hard work put in by the likes of Pasachoff, Zeilik and Shu and their attendant artists and designers.

The three books under review are each in different editions, Shu first, Pasachoff second and Zeilik third. I have no doubt that in a few years time it will be second, third and fourth. Pasachoff and Zeilik have been carefully polished and the problems and errors have obviously been ironed out; it is hard to fault them. The audiences of the three books differ too. Pasachoff and Zeilik are intended for non-science majors, the students being assumed to have no background in mathematics or physics. Shu's, by contrast, do.

Pasachoff describes astronomy in clear, thorough and colloquial terms. Lots of students take astronomy because they have heard about all the fascinating new phenomena and thirst for more; Pasachoff will provide them with a refreshing drink. Students are often non-science majors because they are troubled by physics and mathematics. Pasachoff doesn't add to their worries; after reading his book they will have enjoyed themselves, have been exposed to many new experiences but not, I think, to science. This is one of the reasons

why I prefer Zeilik and why I envy the students of Astronomy 10S at Berkeley. Zeilik's picture of astronomy abounds with science and the science is integrated with the descriptive passages in an unobtrusive way, in the form of focus blocks and detailed illustrations. The student quickly tastes the real flavour of hard science and it is no wonder that the book is now in its third edition.

Shu is different. First he changes the balance, and the coverage of the Solar System drops to 15 per cent as opposed to 24 per cent and 32 per cent in Zeilik and Pasachoff. He has also left the non-science major behind and produced a book which tangles with mathematics and physics.

Problems are scattered throughout the chapters and not clumped in an easily overlooked block at the end; the mind is continually challenged, and on finishing the book you feel as if you have been educated as opposed to merely amused.

Some things worry me, however. I find it rather confusing to call the Sun a low-mass star when it is more massive than about 95 per cent of its near neighbours. And while in this section of the book, a Hertzsprung-Russell diagram of "nearby stars" is awash with giants and supergiants and gives no indication of the real distribution of stellar types in the vicinity. The index could also do with beefing up — it's one thing to provide a good photograph of Abell 1367 but if

you forget where it is you have to flip through lots of pages to find it. But these are minor points which can be easily sorted out for the next edition. My main impression is that Shu has approached the subject in a fresh way, has done an extremely good job and has produced a book to be proud of. Just the thing for a first-year university science course.

Briefly putting the books into the British context, I would give Pasachoff to the third form at school, Zeilik to the O-level physics stream and Shu to the Upper Sixth and university subsidiary classes. □

David W. Hughes is a Lecturer in Astronomy and Physics at the University of Sheffield.

Good weather across the Atlantic

P.A. Smithson

Understanding our Atmospheric Environment, 2nd Edn.

By Morris Neiburger, James G. Edinger and William D. Bonner.

W.H. Freeman: 1982. Pp.450.

\$21.95, £16.30.

The Atmosphere: An Introduction to Meteorology, 2nd Edn.

By Frederick K. Lutgens and Edward J. Tarbuck.

Prentice-Hall: 1982. Pp.478.

\$26.95, £24.25.

General Climatology, 4th Edn.

By Howard J. Critchfield.

Prentice-Hall: 1982. Pp.452.

\$26.95, £24.25.

Atmosphere, Weather and Climate, 4th Edn.

By Roger G. Barry and Richard J. Chorley.

Methuen: 1982. Pp.392. Hbk £14.50,

\$27; pbk £6.50, \$12.95.

WHENEVER a theme becomes fashionable, a plethora of books appears to satiate the resulting appetite for information. In the case of books about the atmosphere, there are now a large number, new and old, good and bad, but the four reviewed here are already well-established and are now appearing as second or fourth editions. Clearly all have shown that their content and approach are satisfactory, but have they adapted adequately to new ideas, techniques and concepts?

All four books are introductory texts, assuming little knowledge on the part of the reader, yet maintain scientific accuracy without the need for detailed technical or mathematical arguments. *Understanding our Atmospheric Environment*, *The Atmosphere* and *General Climatology* are written by Americans mainly for students majoring in subjects other than a physical science and all have a strong American emphasis. The fourth book, *Atmosphere*,

Weather and Climate, is more of a hybrid with an American (by residence, though not by birth or education) and a British author. It aspires to a similar market but aims more specifically at introductory courses on weather and climate in college or university geography departments and in school sixth-forms.

Despite similarities the books do have different emphases. *The Atmosphere* and *Understanding our Atmospheric Environment* might be expected, from their titles, to be concerned solely with meteorology with little consideration of climatology. In general this is true of *Understanding our Atmospheric Environment*, which has only brief sections on climate, but Lutgens and Tarbuck do devote two chapters to the topic, one of which is a traditional and rather dated view of world climates based on the Köppen system. It has the appearance of an after-thought, added to give a wider appeal to the book. The title of *Atmosphere, Weather and Climate* suggests more of a balance between climatology and meteorology. This is achieved by viewing climate from a dynamic point of view, as the result of interactions between the global atmospheric circulation and the Earth's surface with its widely different characters of land and ocean, mountains and plains. Small-scale climate and climatic variability are also included. Of all the books *General Climatology* places greatest stress on climatology alone, with four chapters on the physical basis of climate and four more on regional climatology which precede an examination of a wide range of applications from climatic change to climate and water resources and human bioclimatology.

Which book is preferable for a course depends upon how well each follows course requirements. All are well written and clearly illustrated with diagrams and photographs. Up-dating has been considerable — even Mt St Helens appears, as well as details of current levels of carbon dioxide. Units, however, remain a problem in all the books; attempts have been made to use SI units but the ancestry of many diagrams is clear when inches, degrees Fahrenheit or langley appear. The text is

less of a problem to update but even here confusion can still arise. A major criticism remains. Where climatic data are given, in none of the books is there any indication of the period represented, despite sections on climatic change which stress variability. Unless the data refer to the same period it is impossible to make proper comparisons.

Overall these are four very useful texts which in their new editions should continue to satisfy most courses dealing with the atmosphere and climatology. □

P.A. Smithson is a Lecturer in the Department of Geography at the University of Sheffield.

Understanding the ordinary

M.S. Longair

Extragalactic Astronomy: Lecture Notes from Cordoba.

By J.L. Sérsic.

Reidel: 1982. Pp.260.

Dfl. 120, \$49.50.

ANYONE who has attempted to give a lecture course on extragalactic astrophysics knows that it is among the most difficult of all topics to discuss in a satisfactory way. Not only is the scope of the subject vast but the objects which should form the basis of any such course, the normal galaxies, are those about which many of the data are least secure or totally absent. Given this, what hope have we of understanding their more exotic cousins such as Seyfert galaxies, radio galaxies, quasars and BL-Lac objects?

Professor Sérsic's answer to the methodological problem is given in the book under review, the fruit of about 20 years lecturing on the topic. Any idea that such an approach would lead to a book 20 years out of date can be immediately rejected — one of the admirable features is that the references are many and remarkably up to date. Professor Sérsic writes from the point of view of an optical

astronomer whose prime concern is to understand the ordinary objects in the Universe rather than the exotic. This is reflected in the balance of the chapters. Four of them describe the ordinary stuff out of which our Universe is made — “Forms and Structures”, “Normal Galaxies”, “Galaxies and their Environments”, “Measuring the Universe”. One is entitled “Active Galaxies” and the two remaining main chapters, “Cosmology” and “Gravitational Instability and Galaxy Formation”, discuss cosmological questions.

The advantages and disadvantages of the programme are obvious. First of all, as a lecture course, it has the advantage that the statements made have to be rather definitive or the course would never finish on time. Professor Sérsic’s approach is to outline the main features of each topic and then quote without comment additional facts, alternative interpretations or problems. It works well, provided one is aware that every definitive statement should be subject to a fairly large number of provisos.

I find the sections on normal galaxies very useful and they can be entrusted to beginners in the subject, with the recommendation that this is an introduction and should not be taken as gospel or the last word. The chapter on active galaxies is perhaps the least satisfactory because this is now an enormous field. To consider a subject close to my own heart, the few pages devoted to strong radio galaxies barely begin to address the astrophysical problems one would hope students would be exposed to. The astrophysics of massive black holes in active galactic nuclei is only hinted at, yet it is surely one of the most significant pieces of “new” astrophysics in extragalactic astronomy. The chapters on cosmology and gravitational collapse are straightforward and cover many basic topics in a short space.

I like this book, although the translation is what I will generously call idiosyncratic. I will recommend it to my students as an example of the way in which a classical optical astronomer approaches the problem of expounding what he considers it essential that students should know about extragalactic astronomy. Ideally, it should be read in parallel with similar books by astronomers whose home territories are in the radio, millimetre, infrared, X- and γ -ray wavebands, as well as one by a pure theorist. Professor Sérsic, however, has the advantage of being the one who has most to say about the ordinary components which make up our Universe. □

M.S. Longair is Director of the Royal Observatory, Edinburgh.

Paper comets

New in paperback from Cambridge University Press is John Brandt and Robert Chapman’s *Introduction to Comets*. The book, which was reviewed in *Nature* 296, 783 (1982), costs £6.95, \$11.95.

Up with the times

Michael Rowan-Robinson

Introduction to Special Relativity, 2nd Edn.

By Wolfgang Rindler.

Oxford University Press: 1982. Pp. 184.

Hbk £15, \$39; pbk £6.95, \$13.95.

An Introduction to Tensor Calculus, Relativity and Cosmology, 3rd Edn.

By D.F. Lawden.

Wiley: 1982. Pp. 205. Hbk £14.75, \$33.50;

pbk £6.75, \$14.95.

Seventeen Simple Lectures on General Relativity Theory.

By H.A. Buchdahl.

Wiley: 1982. Pp. 174. £21.25, \$31.85.

Physics of Stellar Evolution and Cosmology.

By Howard S. Goldberg and

Michael D. Scandron.

Gordon & Breach: 1982. Pp. 390.

\$59.50.

FIFTEEN years or so ago when I began to give an undergraduate course on relativity and cosmology, there were two books which my students and I found very useful — Wolfgang Rindler’s *Introduction to Special Relativity* and D.F. Lawden’s *Introduction to Tensor Calculus and Relativity*. It is quite a pleasure therefore to welcome completely new editions of these books, each of which has done such a lot to make relativity theory accessible to the student of general physics or applied maths.

The subject of relativity has changed greatly over the two decades since the first versions of these books appeared. Rindler brings us up to date with these new developments, for example the many experimental tests of relativity, the resolutions of the so-called paradoxes such as the twins paradox, and the appearance of an object moving close to the speed of light. Above all Rindler gives us the deeper physical understanding of special relativity which has grown out of the past 20 years of intensive work on relativity theory. This will be a really useful book for students for years, perhaps decades, to come.

Lawden has written a completely new chapter on the mathematical aspects of cosmology and this certainly extends the scope and usefulness of his book. However he has made remarkably few changes to the chapters on special and general relativity, and as a result the book now has a rather old-fashioned feel. The use of an imaginary time coordinate, for example, will certainly be frowned on by pukka relativists. I think that many lecturers on relativity will be disappointed that this new edition is not more radically revised. I would not be surprised, though, if the less high-flying student continued to find the book useful.

H.A. Buchdahl’s *Seventeen Simple Lectures on General Relativity Theory* are actually quite heavy going. They will probably be more useful to the lecturer on relativity who wants to meditate on the more

esoteric points of the theory than to the student; this is definitely not a book from which one could learn relativity and the lectures read more like a commentary than an exposition. They may appeal to the student for whom the philosophy of science is a major interest and for whom physics and the real world are of secondary importance. The lecture format, with no division into sub-headings, is extremely opaque and it takes some time to get into the book.

Nevertheless by the time I reached the end Buchdahl had convinced me that there was a good deal here that I ought to know and understand. You would have to be one of general relativity’s Mighty Handful not to learn something from these lectures. I disagree with Buchdahl, incidentally, that general relativity’s failure to specify the large-scale topology of the Universe is unimportant. To me this seems a serious incompleteness of the theory and in the past such incompletenesses in physical theory have, in the long run, usually required major new ideas to deal with them.

Elementary particle physicists tend not to regard astronomy as a branch of science at all. It is not surprising, however, that two such physicists, Howard Goldberg and Michael Scandron, should want to write a book on *The Physics of Stellar Evolution and Cosmology* — astronomy has become a tremendous laboratory for all aspects of physics and this book ought to have been a good idea. I think, however, that it suffers from trying to aim at too many audiences at once. In their preface, the authors say the book is written for “the liberal arts and engineering student who has been bitten by the physics bug . . . the graduate science student who wants to obtain a solid foundation: the amateur astronomer who would like to understand more about what he sees”. Such a wide constituency is, of course, impossible to please. The number of equations and the level of physical knowledge assumed mean that the book is completely unsuitable for the non-science major or amateur astronomer, and might even pose problems for final-year science students. At the same time nothing seems to be explained or derived thoroughly and the order-of-magnitude argument is decidedly overworked.

Still, modern accounts of stellar evolution with a strong physical bias are thin on the ground. This book will find its supporters, although the fairly cavalier treatment of astronomical facts and arguments will lose it a few too. A nice feature is several quite amusing cartoons, including the well-known one with two bearded and robed figures sitting on a cloud with one saying “The Big Bang? Believe me, it was very, very, very, very Big”. □

Michael Rowan-Robinson, currently working on the IRAS project at the Jet Propulsion Laboratory in Pasadena, is Reader in Astronomy at Queen Mary College, University of London.

Relativity different

John D. Barrow

General Relativity: An Introduction to the Theory of the Gravitational Field.

By H. Stephani.

Cambridge University Press: 1982.

Pp.310. £25, \$49.50.

AS TIME goes on, it actually becomes easier to write a good textbook on general relativity. You simply follow closely the successful features of the many previous expositors. Some of the most successful relativity textbooks clearly owe much to this type of directed natural selection; with only one or two honourable exceptions, modern texts do not stray very far from the well-worn path found first by Einstein and then mapped by Eddington in his classic *The Mathematical Theory of Relativity*.

In order to justify its existence, any new book (or, as in this case, any translation of an older book) must display genuinely positive features rather than merely fail to exhibit negative ones. By this criterion alone Hans Stephani's concise text more than justifies its publication. It provides a fuller exposition and wider range of topics than, say, Landau and Lifshitz, whilst providing more insight into their content than purely "algebraic" expositions such as Weinberg's *Gravitation and Cosmology*. However, unlike the latter, it has little to say about cosmology.

Stephani provides straightforward and well-organized introductions to many topics normally regarded as beyond the scope of introductory texts. In particular, one finds spinors and tetrads, Lie derivatives, Petrov's classification, plane waves, homogeneous spaces and Bianchi types, the Reissner-Nordstrom metric, together with instructive and non-standard sections on the Cauchy problem and gravitational waves. Also included are some discussions of exact solutions that differ from the usual textbook fodder; for example, the Weyl and axisymmetric vacuum space-times. My only reservations are that the section on the Kerr solution is slightly perfunctory, especially in the light of the space given to other, less important, topics. Also, out of personal prejudice, too little space is allocated to cosmology.

This is an ideal book for a one-term or one-semester graduate course on general relativity, and it also contains material suitable for presentation in undergraduate courses. It is slightly directed towards the mathematician rather than the physicist, but it refrains from the use of exterior calculus and coordinate-free techniques which should make it quite accessible to physicists or astronomers. Whatever their level or background, however, all potential buyers would welcome a cheaper, paperback edition. □

John D. Barrow is a Lecturer in Astronomy at the University of Sussex.

The new synthesis at school

John Mann

Guidebook to Organic Synthesis.

By R.K. Mackie and D.M. Smith.

Longman: 1982. Pp.332. £9.95, \$19.95.

Fundamentals of Preparative Organic Chemistry.

By R. Keese, R.K. Müller and

T.P. Toube.

Ellis Horwood/Halsted: 1982. Pp.146.

Hbk £15, \$42.95; pbk £6.50, \$19.95.

Fundamentals of Organic Chemistry.

By T.W. Graham Solomons.

Wiley: 1982. Pp.830.

Hbk £24.80, \$37.20; pbk £12; \$19.30.

ALMOST two decades have passed since E. J. Corey introduced the term "synthon", and discussed methods for the "disconnection" of synthetic targets to provide a "retrosynthetic analysis" of the problem. These ideas have revolutionized the way in which chemists think about synthesis, but little of this has permeated into undergraduate textbooks. Stuart Warren's *Designing Organic Synthesis: A Programmed Introduction to the Synthon Approach* (Wiley, 1978) provides an excellent account of retrosynthetic analysis,

but makes no attempt to cover synthetic methods (though publicity for his new book *Organic Synthesis: the Disconnection Approach* indicates that the remedy is at hand).

Mackie and Smith's new book thus represents a notable advance in the teaching of organic synthesis to undergraduates, since it interweaves synthetic methodology with retrosynthetic analysis.

After a very brief introduction, the authors deal with functionalization of various acyclic and cyclic systems, then move on to functional group interconversions. Most of the methods discussed are standard, but a few more exotic ones are also included. There follow three chapters on carbon-carbon bond formation. The first of these introduces the terms "synthon" and "disconnection" during a discussion of the strategy of synthesis, and then provides a list of key electrophilic and nucleophilic species which can be employed to effect carbon-carbon bond formation. This leads naturally to in-depth accounts of organometallic compounds and of carbanions; in the former chapter there is comprehensive coverage of Grignard reagents and organocopper compounds, and at the end there are a number of synthetic problems with analyses using the synthon/disconnection approach.

Chapter 5 is lengthy and contains an excellent account of the use of stabilized car-

banions and related species (including phosphorus and sulphur yields), again concluding with useful problems and analyses. The formation of carbon-hetero bonds is covered next, and then Chapter 7 deals at length with ring-closure and ring-opening. Baldwin's rules are mentioned (probably for the first time in an undergraduate text), and a useful account of heterocyclic ring synthesis is followed by a long section on cycloadditions and electrocyclic processes. Regioselectivity and stereoselectivity are discussed in terms of the frontier orbital approach, but for a more detailed treatment readers should go to the latest edition of Sykes's *Guidebook to Mechanism in Organic Chemistry* (for review see *Nature* 295, 487; 1982). This strategem is employed throughout the book, and ensures that the flow of the text is not disturbed by complex mechanistic arguments.

Chapters 8 and 9 deal with reduction and oxidation respectively, and all of the common methods are included. Four short chapters are then devoted to protection of functional groups, organoboranes and their transformations, and phosphorus and silicon reagents in synthesis. The information is more than adequate for undergraduate courses, though sulphur and selenium reagents might have been given an additional chapter. The book concludes with six synthetic problems, providing retrosynthetic analyses and an examination of various routes reported in the research literature — lengthy accounts of steroid and peptide synthesis are included.

Throughout the book references and useful notes appear, and lists of further reading are provided. The authors have successfully arranged a marriage of synthesis and retrosynthesis for the undergraduate reader. Only time will tell whether this book or Stuart Warren's new one will be the more successful.

The book by Keese *et al.* is a useful compendium of basic laboratory methods and techniques, and ranges from essential first-aid and laboratory safety through to hints on the synthesis of radiolabelled compounds. It has valuable sections on the use of the research literature, report writing, purification of solvents, and structure elucidation using spectroscopic methods, and on all of the common methods of extraction and purification. The account is up-to-date (flash chromatography is, for example, included), enlivened by amusing cartoons, and the student edition is excellent value for money.

Finally, the second edition of Solomons's *Organic Chemistry* was reviewed two years ago (*Nature* 289, 721; 1981) and his new text is simply a slight condensation of that book. There are 240 or so fewer pages, about half of this being due to the deletion of special topics sections. The new book is, however, cheaper — so you makes your choice and pays your money. □

John Mann is a Lecturer in Organic Chemistry at the University of Reading.

Atoms and molecules

W. Graham Richards

Physics of Atoms and Molecules.

By B.H. Bransden and C. Joachain.

Longman: 1982. Pp.690.

£12.50, \$26.

The Shape and Structure of Molecules, 2nd Edn.

By C.A. Coulson.

Oxford University Press: 1982. Pp.94.

Hbk £10.95, \$19.95; pbk £4.95, \$8.95.

Computational Chemistry: An Introduction to Numerical Methods.

By A.C. Norris.

Wiley: 1982. Pp.452. Hbk £21.75,

\$50.60; pbk £9.65, \$21.45.

AN OLD classic does not used to tease younger colleagues by demanding an explanation of the difference between chemical physics and physical chemistry. One possible response was to say that the physicists were more interested in atoms while the chemists concentrated on molecules.

Certainly, in *Physics of Atoms and Molecules* Bransden and Joachain devote all but two of their 14 chapters to atoms. The early parts of the book summarize relevant quantum mechanics and give a good undergraduate account of atomic structure. Later chapters cover atomic and electron-atom collisions, and the final section describes some of the important applications of atomic physics. The level is suitable for second- and third-year undergraduates reading physics at a British university and for chemists taking options in chemical physics. The book would not be suitable as a background text of molecular structure for chemistry undergraduates. In the United States it might fall between stools, being too comprehensive for a typical undergraduate course but not sufficiently deep for graduate students.

McWeeny's update of the late Professor Coulson's undergraduate text on molecular structure is, by contrast, very much meat for an undergraduate chemist. Atoms are treated in the briefest possible way whereas molecules are allowed to contain several atoms, even those from the transition series.

The first edition provided a clear if somewhat terse introduction for the first-year undergraduate to the question of why molecules of a given atomic constitution adopt a particular shape. In this second edition some of the introductory material has been amplified and the coverage has been extended to incorporate transition-metal compounds and to make the student aware of the impact of quantitative theoretical calculations. The treatment is intentionally pictorial and qualitative, and none the worse for that. Just occasionally one feels, however, that giving half the story does create the possibility of confusion or misunderstanding. The nature of hybridization is not really understandable without

going into the determinantal nature of orbital wavefunctions: it is seen as an effect rather than a description. On the other hand the combined authority of Coulson and McWeeny is such that the simplified story comes over well enough to enable the student to understand a lot about molecules for a very small investment of effort, and to go on to other chemical problems before returning to make a more detailed and possibly quantitative investigation of molecular structure.

Quantitative studies of molecular structure using molecular orbital techniques have, thanks to developments in computing power, grown into the new sub-discipline of computational chemistry. At the research level this is frequently done using freely available standard packages. Prior to Norris's *Computational Chemistry*, however, there has been very little available for undergraduates and graduate students who have the need or desire to delve into the workings of the programs. It

is increasingly important for chemists to have some basic knowledge of the theory as well as the practice of numerical computation, and this is exactly what the book provides, including an introduction to the Numerical Algorithms library. After basics the areas covered are non-linear equations, simultaneous linear equations, numerical integration, differential equations and approximations. Ideally a course based on this book would follow one on FORTRAN.

Any student who combined the knowledge of all these three books would be in a powerful position — that of understanding the principles, being aware of good problems and being equipped to solve some of them. □

W. Graham Richards is a Lecturer in Physical Chemistry at Oxford University. Second editions of his books *Ab initio Molecular Orbital Calculations for Chemists* and *Quantum Pharmacology* will appear later this year.

Subject without seam

Colin Upstill

Similarities in Physics.

By John N. Shive and Robert L. Weber.

Adam Hilger/Wiley: 1982. Pp.276.

£9.95, \$27.95.

STUDENTS of physics are almost invariably taught in a structured way, their lectures grouped into courses, each with (ostensibly) a common theme or thread. But more often than not there seems little connection between courses, other than that all are part of "physics" — or "mathematics", or whatever. It is only long after graduation — if ever — that students begin to appreciate how similar many bits of physics are, how often the same equations describe different phenomena — disguised in different notations, and with different variables, even different values for constants, but essentially the same.

It is rare to find a teacher who attempts to show his students how their fragments of knowledge are related, and even rarer to find a book which seeks to demonstrate explicitly the ubiquity, utility, and power of similarities and analogies in physics. All credit to Shive and Weber for writing a book which does just this, and moreover at a level comprehensible to first-year undergraduates, by whom such insights are so sorely needed.

Like most books, it is not uniformly good; in places the authors lose their grip on the "similarities" theme, and for the occasional chapter the book metamorphoses into a fairly standard, albeit rather descriptive, physics text. But such lapses are instantly forgiven when one learns the connection between a dentist's rubber dam and an electron microscope, or between

webbed feet and bloomed lenses. How differently one appreciates exponential decay when encountered in the context of determining the time of death of a body, rather than in the usual analysis of some idealized system.

It is a great pity that our teaching system is so structured that a book like this is unlikely to be recommended as a course text; I can only hope that many students will be directed to it as collateral reading for the disjoint collection of courses from which they learn physics. □

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Showing the flag

Maurice Rigby

Introduction to Physical Chemistry.

By Arthur M. Lesk.

Prentice-Hall: 1982. Pp.746.

\$30.95, £27.85.

AT LEAST eight general textbooks of physical chemistry are currently competing for students' attention (and cash) in well-stocked university bookshops. Comparisons between them suggest that there is a remarkable general agreement on the basic material which must be covered, and on looking back at older texts it is clear that this has changed relatively little over the past 20 years or so.

There is perhaps now more general emphasis on the central role of quantum mechanics, but coverage of the classic foundation of thermodynamics and the properties of matter remains largely unaltered, and these topics are normally considered in detail. Some changes, however, are discernible. Newer experi-

mental techniques are commonly described, and examples of sophisticated instrumentation are often used in introductory accounts of topics such as reaction kinetics. In addition, an introductory study of symmetry and group theory has been favoured by some, although not all, authors.

Arthur M. Lesk's *Introduction to Physical Chemistry* does not differ radically in content from its predecessors, but is rather shorter than most of them. This brevity has, of course, been achieved at a price — the account of atomic structure and spectra is very short indeed, while the

whole of molecular spectroscopy is allotted less than 30 pages. This is surely not enough, and may make the book unsuitable for some courses. In contrast, the coverage of thermodynamics and solution properties is quite detailed, and many examples are discussed.

Each chapter begins with a study guide identifying topics of particular importance, and many calculations are given, both as illustrative examples and as exercises. A study of the Fourier transforms of the national flags of the United States, Britain and France is particularly intriguing. Several applications of physical

chemistry in biology are described, and this will be welcomed by many readers.

The presentation of the book is generally clear. There is a wealth of diagrams and a novel feature is the inclusion of fairly full references to collections of experimental data. *Introduction to Physical Chemistry* merits serious consideration by those seeking a relatively concise modern text, and for whom the deficiencies noted above are unimportant. □

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Biophysics of course

M.E.J. Holwill

**Physics for the Biological Sciences:
A Topical Approach to Biophysical
Concepts.**

By F.R. Hallett, P.A. Speight and
R.H. Stinson.

Chapman & Hall: 1982. Pp.254.
£9.95, \$22.95.

ALTHOUGH many notable contributions to biology and medicine have been made through a physical approach, many of today's biological science students study no physics during their undergraduate years. One reason often given by students who choose not to enrol on a physics course is that they do not see the relevance of much of physics to the study of biological systems; some physics texts written specifically for biological and medical students do little to alter this view, possibly because a rather traditional approach to the subject is usually adopted, with applications to biology assuming apparently secondary importance.

Physics for the Biological Sciences, a revamped version of *Introductory Biophysics* (1977), is not of this genre. Rather, the authors aim to stimulate a student's interest by posing a question of biological significance before discussing the physical principle which helps to provide the answer. In my opinion, they have succeeded admirably and have produced a book with an informal, easily readable style.

The authors concentrate on the application of physics to biological problems, rather than to instrumentation (there is no mention, for instance, of that ubiquitous biological instrument, the electron microscope), and succeed in covering those areas which are currently of greatest interest. Many worked examples appear in the text and students can test their understanding of a point by attempting the many problems to be found at the end of each chapter (answers are given). Useful appendices on mathematical skills, units, dimensions and waves are provided and could serve as an *aide mémoire* when, for

example, a mathematical point in the text is not clear. The bibliography, while useful, could have been updated, but this is a minor criticism of an otherwise excellent volume.

As is common with books written for a particular audience, *Physics for the Biological Sciences* derives from a course taught in the authors' department. For this

reason others may find it difficult to use the book for their own courses, but it is valuable supplementary reading and some lecturers may consider it worthwhile to modify their courses to suit the text. □

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Quantum physics with a difference

R.B. Jones

**A First Course in Quantum Mechanics,
revised edn.**

By H. Clark.

Van Nostrand Reinhold: 1982. Pp.367.
£5.25, \$12.95.

Basic Quantum Mechanics, 2nd Edn.

By J. M. Cassels.

Macmillan, London: 1982. Pp.200.
Hbk £25, \$38.50;
pbk £12, \$18.50.

Quantum Mechanics.

By Alastair I. M. Rae.

McGraw-Hill: 1982. Pp.246.
£6.95, \$13.95.

**An Introduction to Theory and
Applications of Quantum Mechanics.**

By Amnon Yarov.

Wiley: 1982. Pp.300.
Hbk £23.90, \$35.85; pbk £9.10, \$14.75.

THE EMERGENCE of snowdrops, early crocus and new (or re-furbished) quantum mechanics textbooks indicates that Spring will soon be upon us and that the prudent reviewer, like the conscientious gardener, should take out his pruning shears to inspect and correct the new growth. All of the four texts reviewed here are intended for a first course in the subject, but the refreshing differences amongst them emphasize the vast range of quantum physics.

A new chapter on electrons in solids appears in the revised edition of *A First Course in Quantum Mechanics* in addition to some old misprints and an incorrect statement of the momentum repre-

sentation. All standard applications except the partial wave treatment of scattering are included, as are a good collection of problems for the reader in each chapter. I think the treatment of time-independent perturbation theory relies unduly on the use of determinants which are not well known to present-day undergraduates; moreover, many advanced topics (group theory, Dirac equation, second quantization, solid state theory) are introduced in too brief and superficial a manner to be of great help to a student. This text is useful, but not outstanding, and is better suited to applied mathematics students than to physics undergraduates.

In its second edition, *Basic Quantum Mechanics* includes a new discussion of the qualitative behaviour of wave-functions in one-dimension and a more thorough account of scattering by means of the partial wave S-matrix. I liked the terse prose and the succinct use of operator methods to treat the harmonic oscillator and angular momentum. There are many nice examples from scattering theory, although the partial wave treatment is almost entirely s-wave. The treatment of time-dependent perturbation theory is unduly obscure because only the decay of a state is discussed in detail — a student would not be able to see readily how atomic populations in a laser may oscillate rather than simply decay. The mention of some standard atomic structure problems (e.g. the helium atom) is also too curt to convey much to a student. This is nonetheless a good book for a first course for physics students — but the lecturer would have to supplement the text on several topics.

Quantum Mechanics is a new text suitable in scope for a first course on one-particle quantum mechanics. I found the introductory chapters dull but the later

discussion of well-chosen physical examples is much more interesting. There is almost no use of operator methods, the emphasis being on differential equation techniques instead so that the book could be used very early in an undergraduate course. I noted a misleading suggestion — that there is a freedom of sign in the momentum operator — and an incorrect assumption — that time is an observable on the same footing as the position observable — but welcome the unusual final chapter. This summarizes in a clear and readable way different points of view about measurement theory in quantum mechanics, and includes a simple illustration of the point of Bell's theorem.

An Introduction to Theory and Applications of Quantum Mechanics is meant for students interested in applied physics and those topics commonly called

quantum electronics. The first half of the book is an uninspired standard introduction, using mainly differential equation methods and omitting any discussion of three-dimensional scattering. The later parts of the book, however, are rather exciting as the author treats applications which interest him personally, including laser oscillation, magnetic resonance, charge transport in semiconductors, p-n and p-n-p junctions, and semiconductor injection lasers. The discussion of these topics is excellent and is conducted at a well-judged quantitative level. I would not use this as a main text for a first quantum mechanics course but it would be a splendid choice for the student embarking on applied quantum physics. □

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Playing at farming for real in the Third World

Graham Farmer

The Green Revolution Game.

Available from Marginal Context,
36 St Andrew's Road, Cambridge
CB4 1DL, UK.
Price £195 + VAT.

"DROUGHT in the flowering season. Patel farm has a pest attack on high yielding rice varieties. . .".

The object of *The Green Revolution Game* is to simulate life in an Indian farming village, focusing on rice production both for feeding the farm workers and marketing of the surplus. Participants, normally grouped in pairs, take the role of farmers. The game is controlled by an impartial manager and a banker/trader/money-lender, whose level of honesty varies according to preference. Weather, pest attack and birth rates are determined by the manager, but the rest of the game depends on the players — social structures, economic systems, even crime rate and corruption levels are all dependent on their decisions. There is, therefore, endless scope for variety, and every run of the game is different.

Statistics upon which the game is based were collected in South Bihar, India, by Graham Chapman of Cambridge University. His experience has been combined with that of Elizabeth Dowler and Philip Payne, both of the London School of Hygiene and Tropical Medicine, to produce a standard kit. After backing from the National Westminster Bank, under the Government's small firms loan guarantee system, 1,000 kits were produced and launched late last year.

In a run of the game, random initial conditions of farm size and family size produce a labour market. The game then simulates growing seasons, normally six, each of which is split into three parts. Rice yields are determined by weather throughout the season, frequency of pest attacks, and application of modern technology in the form of irrigation, fertilizer and pesticide. Such technology has to be bought from the banker by selling surplus rice or raising a loan. Weighing against such investment is the need to feed the farm workers and their families — if a rice deficit exists, people may die.

After the simulated growing seasons the players discuss their actions and decisions. It is this detailed analysis that moves *The Green Revolution Game* from just a game to a "learning experience". Participants can see how the social and economic structures changed throughout the game, with different benefits and problems arising from such factors as initial land/labour ratios and availability of labour. Not only can performance of individual farms be assessed, but also that of the village unit as a whole.

The game is fun to play and simulates well the problems experienced by farmers in the Third World. It is designed for six to twelve farms, and the game improves as the maximum is reached. However one successful run of the game in Nigeria used fifteen farms with four people to each farm. Potential players range from students to professionals involved in development projects. The kit itself is comprehensive, with a large package containing model people, pesticide, fertilizer and rice tokens, and supplies of paper money and industrial bonds. If the price seems expensive, stop thinking of it as a game and consider it again as a teaching aid. □

Graham Farmer is a Senior Research Associate in the Climatic Research Unit, University of East Anglia.

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CRAWFORD, M.H. and MIELKE, J.H. (eds). *Current Developments in Anthropological Genetics*, Vol.2: *Ecology and Population Structure*. Pp.525. ISBN 0-306-40842-2. (Plenum: 1982.) \$59.50.

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CREUTZBELDT, W. (ed.). *Acarbose: Effects on Carbohydrate and Fat Metabolism. Proceedings of the 1st International Symposium held October 1981, Montreux*. Pp.573. ISBN 90-219-9540-9/0-444-90283-X. (Excerpta Medica/ Elsevier Science/North Holland: 1982.) \$80.75, Dfl. 190.

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DRYHURST, G., KADISH, K.M. *et al.* *Biological Electrochemistry*, Vol.1. Pp.548. ISBN 0-12-222401-9. (Academic: 1982.) \$74.

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FINEGOLD, S.M. and MARTIN, W.J. Bailey and Scott's *Diagnostic Microbiology*, 6th Edn. Pp.705. ISBN 0-8016-1577-1. (C.V. Mosby: 1982.) Np.

Appointments

James Rainwater, who shared the 1975 Nobel Prize in Physics for his work in describing the shape of the atomic nucleus, has been named Pupin professor of physics at Columbia University.

Sir Kenneth Berrill is to be the new pro-chancellor of the Open University, UK, and chairman of the University Council, its governing body.

Dr Barry Brady will succeed the late Dr D.F. Kelsall as chief of the division of applied geomechanics of the Commonwealth Scientific and Industrial Research Organization (CSIRO), based in Melbourne, Australia.

An Australian physicist, **Professor Neville Fletcher**, has been appointed to head CSIRO's Institute of Physical Sciences.

The University of Salford in conjunction with two British industries, British Aerospace and British Gas, has set up the first two integrated chairs in Britain, designed to increase collaboration with industry. **Bernard Heath**, OBE, is the first to be appointed to the British Aerospace chair in aeronautical engineering in the department of aeronautical and mechanical engineering. **Geoffrey Roberts**, CBE, has been appointed to the British Gas chair in gas engineering in the department of chemical engineering.

Dr B.W.E. Alford has been appointed professor of economic and social history at the University of Bristol, UK. He succeeds Professor W. Ashworth.

The dean of the Royal Postgraduate Medical School, University of London, **Dr Malcolm Godfrey**, has been appointed second secretary of the Medical Research Council.

The University of Hull, UK, has established an Institute of Estuarine and Coastal Studies, and has chosen **Dr Neville Jones** to be its director.

A Medical Research Council clinical research professorship has been awarded to **Dr A.J. McMichael** who is a university lecturer in medicine at the Nuffield department of clinical medicine, University of Oxford.

Dr Julian Davies has been appointed president of Biogen, the international biotechnology company.

Dr Peter Kemp has been appointed director of Reading University's computer centre.

Dr Carlyle Guerra de Macedo has been made director of the Pan American sanitary bureau and of the regional office of the World Health Organization.

The British Oxford Instruments Group has appointed **Dr Peter Williams** as executive director of its analytical division. Dr Williams is responsible for two companies within the group, Oxford Research Systems Limited and Oxford Analytical Instruments Limited.

Richard Butler has recently taken up office as the secretary general of the International Telecommunication Union.

Miscellaneous

The registration fee for the XV International Congress of Genetics has been reduced from \$300 to \$200 for full members only.

A series of video-taped lectures on various aspects of pressurized water reactors (PWRs) given by senior scientists and engineers from the British nuclear industry is now available to the public. The two lectures presently available are "The design and safety of the Sizewell PWR", given by Sir Walter Marshall, Chairman of the Central Electricity Generating Board, and suitable for general audiences, and "Operational transients for the PWR including loss of coolant accidents", a technical lecture given by John Collier, head of the UKAEA Safety and Reliability Directorate. Further details are available from Viscom Ltd, Park Hall Road Trading Estate, London SE21 8EL, UK.

Papers are invited for the Analyticon '83 Conference which is being held in association with the Laboratory '83 Exhibition in London from 12 to 14 October 1983. The conference will cover all aspects of analytical chemistry, clinical science and surface physics and it is hoped to include papers on organic structure, chromatography, and elemental analysis, although any related subject will be considered. Papers should be sent to the Scientific Instrument Manufacturers' Association, Leicester House, 8 Leicester Street, London WC2H 7BN, UK, preferably before 31 March 1983.

Papers and posters are invited for the 10th International Symposium on the Biological Characterization of Human Tumours—**Cancer Chemotherapy and Selective Drug Development** to be held in Brighton, UK from 24 to 28 October 1983. Details of the themes covered by the symposium and registration or abstract forms can be obtained from CCHTI Secretariat, Institute of Cancer Research, Block E, Clifton Avenue, Belmont, Sutton, Surrey SM2 5PX, UK.

Awards

The 1982 Gold Medal, presented by the French National Centre of Scientific Research for outstanding scientific research, has been awarded to **Professor Pierre Joliot** of the department of cellular bioenergy, Collège de France.

The Zoological Society of London has announced the following awards. **Dr R.M. Anderson** of the Imperial College of Science and Technology, University of London, **Dr P.J. Butler** of the University of Birmingham and **Dr J. Cooke** of the National Institute for Medical Research, Mill Hill have received the Society's Scientific Medal; **Professor J.M. Dodd** has been awarded the Zoological Society of London Frink Medal for British Zoologists. **Dr G.R. Spedding** of the University of Bristol has received the Thomas Henry Huxley Award; **R.M. Gambles** has received the Stamford Raffles Award for amateur zoologists; and the Prince Philip Prize, awarded for practical work conducted by a pupil under the age of 19 has been given to **Paul Stewart** of Merchant Taylors' School, Northwood.

Dr Reen Wu, a research chemist at the National Institute of Environmental Health Science at Research Triangle Park, North Carolina, has received the first Research and Development Award of the W. Alton Jones Cell Science Centre.

Daniel Perez, the University of California at San Francisco's assistant professor of medicine at San Francisco General Hospital, has received a five-year established investigatorship award from the American Heart Association to continue his research into arthritis.

Bell Laboratories have named three of their own scientists as recipients of the first Bell Laboratories Fellowships Awards for their contributions in solid state devices, satellite communications and lightwave technology. **Harold Boll**, **Donald Duttweller** and **John MacChesney** are to receive the awards.

Applications are invited for the Gunnar Nilsson Cancer Research Trust Fund, an award of up to £15,000 given to assist cancer research projects where money is not available from the normal grant-giving bodies. Applications should take the form of an abstract, five copies of which should be submitted to Dr Norman Howard, Chairman — Gunnar Nilsson Cancer Research Trust Fund, Department of Radiotherapy and Oncology, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, UK.

Meetings

6-7 April, **Agriculture and the Food Industry — A Partnership for Progress**, Reading (The Conference Secretariat, SCI, 14-15 Belgrave Square, London SW1X 8PS, UK).

11-13 April, **Annual Chemical Congress**, Lancaster (Dr John Gibson, The Royal Society of Chemistry, Burlington House, London W1V 0BN, UK).

11-14 April, **International Conference on Combustion in Engineering**, Oxford (G.V. Williams, Press and Information Officer, The Institution of Mechanical Engineers, 1 Birdcage Walk, Westminster, London SW1H 9JJ, UK).

11-15 April, **International Symposium on Biological Effects of Low-Level Radiation — Stochiometric and Non-Stochiometric Effects**, Venice (International Atomic Energy Agency, PO Box 100, Vienna International Centre, A-1400 Vienna, Austria).

12-14 April, **Reliability Risk Management Techniques for the Offshore Industries**, Stavanger (Ms Helen Raquet, Assistant Conference Organizer, Oyez Scientific and Technical Services, Bath House (3rd Floor) 56 Holborn Viaduct, London EC1A 2EX, UK).

12-15 April, **Stabilization and Disinfection of Sewage Sludge**, Manchester (Mr Eric Porter, Conference Organizer, Water Research Centre, Medmenham Laboratory, PO Box 16, Henley Road, Marlow, Bucks SL7 2HD, UK).

18-20 April, **Intramolecular Kinetic**, London (Dr John Gibson, The Royal Society of Chemistry, Burlington House, London W1V 0BN, UK).

18-22 April, **Residential School for Mass Spectrometry**, Manchester (Miss L. Hart, Royal Society of Chemistry, 30 Russell Square, London WC1B 5DT, UK).

18-22 April, **International Symposium on Isotope and Radiation Techniques in Soil Physics and Irrigation Studies**, Aix-en-Provence (International Atomic Energy Agency, PO Box 100, Vienna International Centre, A-1400 Vienna, Austria).

19-21 April, **Exhibition of Numerical Engineering Equipment and Services**, London; to be held in conjunction with the **Numerical Engineering Society's Technical Conference**, (20-21 April), (The Manager — Conferences and Exhibitions, The Institution of Production Engineers, Rochester House, 66 Little Ealing Lane, London W5 4XX, UK).

21-22 April, **Symposium on Advanced Analytical Concepts for the Clinical Laboratory**, Gatlingburg (Ms Marjorie Hack, Public Information Director, American Association for Clinical Chemistry, 355 St Paul's Avenue, Staten Island, NY 10304, USA).

2-5 May, **Colloquium on Protides of the Biological Fluids**, Brussels (Colloquium Secretariate, c/o Lipid and Protein Department, Chaussee d'Alsebergsesteenweg 196, B, 1180 Brussel, Belgium).

9-13 May, **Joint Congress of the European Tissue Culture Society and the European Reticuloendothelial Society**, Budapest (A.T. Gyévai, Institute of Experimental Medicine, Laboratory for Tissue Culture, Hungarian Academy of Sciences, H-1083 Budapest, Szigony u. 43, Hungary).

9-13 May, **Oil Pollution Course**, Ipswich (Miss C.H. Little, The Institute of Petroleum, 61 New Cavendish Street, London W1M 8AR, UK).

10 May, **Toxicology — Training and Evaluation Needs for Biologists and Chemists**, London (Dr C.S. Collis, 46 Lyndhurst Road, London N22 5AT, UK).

15-21 May, **Joint Meeting of the European Chapters of the International Association for the Study of Pain**, Padova (Dr Ruggiero Rizzo, Ospedale Regionale, 36100 Vicenza, Italy).

17-18 May, **Heat Flow in Nuclear and Process Plant Safety**, London (G.V. Williams, Press and Information Officer, The Institution of Mechanical Engineers, 1 Birdcage Walk, Westminster, London SW1H 9JJ, UK).

17-20 May, **CLEO '83, The Conference and Exhibition of Lasers and Electro-Optics**, Baltimore (Tiemo von Zweck, Publicity Chairman, CLEO '83, Laser Power Optics, 11211 Sorrento Valley Road, San Diego, California 92121, USA).

18-19 May, **Residential School on Medium Effects, Crown Ethers and Phase Transfer Catalysis in Organic Synthesis**, Brunel University (Miss L. Hart, Royal Society of Chemistry, 30 Russell Square, London WC1B 5DT, UK).

18-19 May, **Residential School on Emulsions and Microemulsions**, Brunel University (Miss L. Hart, Royal Society of Chemistry, 30 Russell Square, London WC1B 5DT, UK).

19-20 May, **International Symposium on Wave Therapies**, Versailles (Dr Z.W. Wolkowski, Editor, Laboratoire de Physico-chimie et Bioélectromagnétisme, Université de Paris, Val de Marne, 94010 Creteil, France).

23 May, **Lecture on The Recent Development of Atom Resolution Transmission Electron Microscopy**, London (The Administrator, The Royal Microscopical Society, 37-38 St Clements, Oxford OX4 1AJ, UK).

26-27 May, **Application of Computer Systems for Industrial Safety and Control**, Zurich (Ms Helen Raquet, Assistant Conference Organizer, Oyez Scientific and Technical Services, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX, UK).

30 May-3 June, **Spring Meeting of the American Geophysical Union**, Baltimore (American Geophysical Union, 2000 Florida Avenue, NW, Washington, DC 20009, USA).

1-3 June, **ASES '83, Annual Meeting of the American Solar Energy Society**, Minneapolis (American Solar Energy Society Inc, 1230 Grandview Avenue, Boulder, Colorado 80302, USA).

14-17 June, **Acid Rain and Forest Resources Conference**, Quebec City (M Claude Gendreau, Chairman of the Arrangements Committee, Acid Rain and Forest Resources Conference, Laurentian Forest Research Centre, Environment Canada, PO Box 3800, 1080 Route du Vallon, Sainte-Foy, Quebec, Canada G1V 4C7).

3-7 July, **International Congress on Genetic and Epigenetic Interactions in Neural Development**, Salt Lake City (Professor Jean Lauder, Department of Anatomy, 108 Swing Building 217H, University of North Carolina, School of Medicine, Chapel Hill, NC, 27514, USA).

3-8 July, **European Congress and International Exhibition of Clinical Chemistry**, Budapest (Hungexpo, Hungarian Foreign Trade Office for Fairs and Publicity, H-1441 Budapest, PO Box 44, Hungary).

4-8 July, **International Conference on Solid State Ionics**, Grenoble (M. Kleitz, SSI 83, ENSEEG, BP 44, 38401, Saint Martin d'Hères, France).

4-9 July, **International Conference on General Relativity**, Venice (GR10 Secretariat, Istituto di Fisica 'G. Galilei', Via Marzolo, 8, I 35100 Padova, Italy).

11-15 July, **International Conference on The Origin of Life**, Mainz (Secretary 7th ICOL, Ms C. Brand, c/o Institut für Biochemie, Gutenberg Universität, Postfach 3980, D-6500 Mainz, West Germany).

11-16 July, **World Congress of Psychiatry**, Vienna (VII World Congress of Psychiatry, PO Box 9, A-1095 Vienna, Austria).

18-22 July, **International Symposium on Bioelectrochemistry and Bioenergetics**, Stuttgart (Professor H.W. Nurnberg, Secretary General of the Bioelectrochemical Society, Nuclear Research Centre (KFA), Institute for Applied Physical Chemistry, PO Box 1913, D 5170 Jülich, West Germany).

19-22 July, **International Conference on the Clinical Chemistry and Chemical Toxicology of Metals**, Montreal (COMTOX Secretariat, 340 MacLaren Street, Ottawa, Ontario, Canada K2P 0M6).

25-29 July, **International Conference on the Organic Chemistry of Selenium and Tellurium**, Birmingham (Professor W.R. McWhinnie, Department of Chemistry, The University of Aston in Birmingham, Gosta Green, Birmingham BA 7ET, UK).